ORGANIC SYNTHESES

AN ANNUAL PUBLICATION OF SATISFACTORY METHODS FOR THE PREPARATION OF ORGANIC CHEMICALS

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ORGANIC SYNTHESES

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PREFACE TO VOLUME X

THE present volume forms the first annual number in the second decade of this series. A revised collection of the material presented in the first nine volumes is in preparation, so that no attempt has been made to refer to these volumes in the Index. Otherwise, no departure has been made from the general plan adopted in recent numbers, beyond the inclusion of a rather greater proportion of organic preparations of a biochemical rather than a strictly synthetic character.

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ORGANIC SYNTHESES

I

ACETOL

$$HCO_2C_2H_5 + KOH \rightarrow HCO_2K + C_2H_5OH$$
$$CH_3COCH_2Br + HCO_2K \rightarrow CH_3COCH_2OCHO + KBr$$
$$CH_3COCH_2OCHO + CH_3OH \rightarrow CH_3COCH_2OH + HCO_2CH_3$$

Submitted by P. A. Levene and A. Walti.
Checked by Frank C. Whitmore and J. Pauline Hollingshead.

1. Procedure

In a 3-l. round-bottom flask fitted with a 75-cm. Liebig condenser is placed 210 g. of potassium hydroxide (purified with alcohol) dissolved in 1500 cc. of anhydrous methyl alcohol. The solution is cooled to below 50° (Note 1), 300 g. of purified ethyl formate is added and the mixture is refluxed for two hours (Notes 2 and 3).

Then 410 g. (257 cc., 3 moles) of bromoacetone (page 12) is added and the mixture is refluxed for sixteen hours on a water bath at 95–97°. At the end of the operation the solution is cooled to 0° in an ice-salt bath. The potassium bromide which settles out is filtered off on a cooled suction filter and the filtrate is fractionated.

The fraction boiling at 23–35°/12 mm. is discarded, as it contains very little acetol. The main fraction distils at 35–47°/12 mm. and weighs 160 g. This is refractionated. The fraction boiling at 40–43°/12 mm. weighs 120–130 g. (54–58 per cent of the theoretical amount) (Note 4).

2. Notes

1. It is necessary to cool the mixture below 50° to prevent the ethyl formate from boiling out.

2. Technical ethyl formate was purified by washing with 3 per cent sodium carbonate solution, then with cold water, drying over anhydrous sodium sulfate, filtering, and fractionating. It is very important that all the materials used in the synthesis of acetol be anhydrous, as otherwise condensation products are formed.

3. If commercial potassium formate is used it should be dried under reduced pressure at 80°. One and one-half to two moles should be used per mole of the bromo compound.

4. Acetol polymerizes very readily on standing but remains unchanged when dissolved in an equal volume of methyl alcohol.

3. Methods of Preparation

Nef prepared acetol in several ways, the more important of which depended upon the reaction between bromoacetone and potassium or sodium formate or acetate, and the subsequent hydrolysis of the ester by methyl alcohol.[1,2] Acetol is also formed, together with pyruvic acid, by the direct oxidation of acetone by Baeyer and Villiger's acetone-peroxide reagent.[3]

[1] Nef, Ann. **335**, 260 (1904).
[2] Nef, Ann. **335**, 247 (1904).
[3] Pastureau, Bull. soc. chim. (4) **5**, 227 (1909).

II

n-AMYL BENZENE

$$C_6H_5CH_2Cl + Mg \rightarrow C_6H_5CH_2MgCl$$

$$C_6H_5CH_2MgCl + 2\,p\text{-}CH_3C_6H_4SO_3C_4H_9 \rightarrow C_6H_5(CH_2)_4CH_3 + C_4H_9Cl + (p\text{-}CH_3C_6H_4SO_3)_2Mg$$

Submitted by HENRY GILMAN and J. ROBINSON.
Checked by C. S. MARVEL and S. S. ROSSANDER.

1. Procedure

ONE mole of benzylmagnesium chloride is prepared in a 2-l. three-neck round-bottom flask from 24.3 g. (1 mole) of magnesium turnings, 126.5 g. (1 mole) of benzyl chloride and 500 cc. of anhydrous ether, according to the directions given in Org. Syn. **4**, 59. Stirring should be commenced with the first addition of the benzyl chloride. The time of addition of the benzyl chloride in this preparation is about two hours. When all has been added, the mixture is gently boiled for about fifteen minutes (Note 1).

The solution is cooled with running water, and 456 g. (2 moles) of n-butyl p-toluenesulfonate (Org. Syn. **9**, 28) dissolved in about twice its volume of anhydrous ether is then added slowly with stirring through the separatory funnel at such a rate that the ether just boils. The time required for the addition is about two hours. A white solid soon forms and the mixture assumes the consistency of a thick cream. Stirring is continued, without cooling, for about two hours, and the mixture is hydrolyzed by pouring onto crushed ice to which is then added about 125 cc. of concentrated hydrochloric acid (Note 2).

The ether layer is separated and combined with a 200-cc. ether extract of the aqueous layer. The combined ether solution is washed once with about 100 cc. of water and then dried by shaking for a few minutes with about 10 g. of anhydrous

potassium carbonate. After filtration, the ether is distilled on a water bath. When practically all of the ether has distilled, about 5 g. of sodium, freshly cut and in thin slices, is added and the mixture is boiled for about two hours (Note 3). The solution is decanted and then distilled, using an efficient fractionating column. The fraction boiling at 190–210° is collected. This on redistillation yields 74–88 g. (50–60 per cent of the theoretical amount) of *n*-amyl benzene boiling at 198–202° (Note 4).

2. Notes

1. It has recently been shown[1] that benzyl magnesium chloride can be prepared without essential impairment of yield by the rapid addition of benzyl chloride to magnesium in ether.

2. The hydrolysis is preferably carried out in a 5-l. Erlenmeyer flask. The magnesium *p*-toluenesulfonate is sparingly soluble in hydrochloric acid, and complete solution is brought about by the subsequent addition of about 2 l. of water.

3. Refluxing with sodium helps to remove the small amount of benzyl alcohol formed by the atmospheric oxidation of benzylmagnesium chloride.

4. The major part of the *n*-amyl benzene distils at 199–201°. A careful fractionation of the distillate that comes over around 75° yields 24 g. (26 per cent of the theoretical amount) of *n*-butyl chloride boiling at 76–80°.

3. Methods of Preparation

The method described here has been adapted from the directions of Gilman and Heck,[2] and Rossander and Marvel.[3] *n*-Amyl benzene has also been prepared by the action of sodium on a mixture of benzyl and *n*-butyl bromides,[4] and by heating *n*-butyl phenyl ketone and formic acid with copper at 300°.[5]

[1] Gilman, Zoellner and Dickey, J. Am. Chem. Soc. **51**, 1583 (1929).
[2] Gilman and Heck, J. Am. Chem. Soc. **50**, 2223 (1928).
[3] Rossander and Marvel, J. Am. Chem. Soc. **50**, 1491 (1928).
[4] Schramm, Ann. **218**, 388 (1883).
[5] Mailhe and de Godon, Bull. soc. chim. (4) **21**, 62 (1917).

III

BENZENESULFOCHLORIDE

$$C_6H_6 + 2ClSO_3H \rightarrow C_6H_5SO_2Cl + H_2SO_4 + HCl$$

Submitted by H. T. CLARKE, G. S. BABCOCK, and T. F. MURRAY.
Checked by FRANK C. WHITMORE and A. M. GRISWOLD.

1. Procedure

IN a 5-l. flask, fitted with stirrer, dropping funnel, exit tube, and thermometer, is placed 3500 g. (30 moles) of chlorosulfonic acid (Note 1), and to it is slowly added, with continuous stirring, 780 g. (10 moles) of benzene (Note 2), keeping the temperature between 20° and 25° by means of cold water. The hydrogen chloride which is evolved is led to a hood or absorbed in water. The addition requires two to three hours; when this is complete, the mixture is stirred for an hour, and poured onto 6–7 kg. of crushed ice (Note 3). One liter of carbon tetrachloride is then added, the oil is separated as soon as possible (Note 4), and the watery layer is shaken with 500 cc. of carbon tetrachloride. The combined oil is washed with dilute sodium carbonate, and the bulk of the carbon tetrachloride is distilled under atmospheric pressure (Note 5); the pressure is then reduced (Note 6) and the benzenesulfochloride collected at 113–115°/10 mm. (118–120°/15 mm.). The yield is 1320–1360 g. (75–77 per cent of the theoretical amount) of a colorless liquid which on cooling sets to a crystalline solid melting at 13–14°.

A small amount (50–100 g.) of a higher boiling material remains in the flask. This is mainly diphenyl sulfone, which may be isolated by distillation under reduced pressure (b.p. 225°/10 mm.) and recrystallization from methyl alcohol. It forms colorless crystals which melt at 128°.

2. Notes

1. If less than 50 per cent excess of chlorosulfonic acid is taken, the yield of diphenyl sulfone increases at the expense of the sulfochloride.

2. A good commercial grade of benzene, boiling over a 1° range, is satisfactory. The benzene must be added to the acid (not vice versa); otherwise, a larger proportion of sulfone is formed.

3. The benzenesulfochloride separates at first as a crystalline solid which melts as the temperature rises. It was found impracticable to filter off this solid, owing to its tendency to melt on the funnel.

4. The sulfochloride should be removed from the water as soon as possible; otherwise, the yield falls, owing to hydrolysis. In one run in which the mixture was allowed to stand overnight before separating, only 1220 g. (69 per cent) was obtained. If difficulty is experienced in the separation, owing to the presence of suspended solid matter, the oil may first be filtered with suction through a hardened paper or felt cloth. As a rule, it is merely necessary to filter the sludgy layer lying between the oil and the water.

5. The carbon tetrachloride vapor carries with it any moisture that may be present. If this were not removed at a relatively low temperature, hydrolysis of the chloride would take place, with the formation of sulfonic acid which would promote decomposition of the sulfochloride during its distillation.

6. The pressure should be reduced gradually, and the first runnings, mainly carbon tetrachloride, collected separately.

3. Methods of Preparation

The preparation of benzenesulfochloride from sodium benzenesulfonate with phosphorus pentachloride or phosphorus oxychloride has already been described in a previous article in this series,[1] in which a bibliography of the literature is to be

[1] Adams and Marvel, Org. Syn. **1**, 21 (1921).

found. To this bibliography should be added the following references: by the action of phosphorus pentachloride on diphenyl sulfone;[2] by the action of chlorine on benzenesulfinic acid;[3] by the action of phosphorus pentachloride on benzenesulfonic acid;[4] from diphenyl sulfoxide and chlorine;[5] by the action of sulfuryl chloride on benzene in the presence of anhydrous aluminium chloride;[6] by the action of benzene on chlorosulfonic acid, followed by the addition of water.[7] The present process is based on those of Pummerer[8] and of Ullmann.[9]

[2] Gerhardt and Chancel, Jahresb. **1852**, 433; Otto, Ann. **136**, 157 (1865).
[3] Otto, Ann. **145**, 321 (1868).
[4] Mohrmann, Ann. **410**, 379 (1915); Rosenmund and Struck, Ber. **54**, 439 (1921).
[5] Boeseken and Waterman, Rec. trav. chim. **29**, 326 (1910).
[6] Boeseken, Rec. trav. chim. **30**, 382 (1911).
[7] Saccharinfabrik A.G., Ger. pat. 224,386, Frdl. **10**, 114 (1913).
[8] Pummerer, Ber. **42**, 1802, 2274 (1909).
[9] Ullmann, Ber. **42**, 2057 (1909).

IV

BENZOPHENONEOXIME

$$(C_6H_5)_2CO + H_2NOH \cdot HCl + NaOH \rightarrow (C_6H_5)_2C{=}NOH + 2H_2O + NaCl$$

Submitted by ARTHUR LACHMAN.
Checked by C. R. NOLLER.

1. Procedure

A MIXTURE of 100 g. (0.55 mole) of benzophenone, 60 g. (0.86 mole) of hydroxylamine hydrochloride, 200 cc. of 95 per cent ethyl alcohol, and 40 cc. of water is placed in a 2-l. round-bottom flask. To this is added in portions, with shaking, 110 g. (2.76 moles) of powdered sodium hydroxide. If the reaction becomes too vigorous, cooling with tap water may be necessary. After all the sodium hydroxide has been added, the flask is connected to a reflux condenser, heated to boiling, and refluxed for five minutes. After cooling, the contents are poured into a solution of 300 cc. of concentrated hydrochloric acid in 2 l. of water. The precipitate is filtered with suction, thoroughly washed with water, and dried (Note 1). The yield is 106–107 g. (98–99 per cent of the theoretical amount) of a product melting at 141–142°. On crystallizing 20 g. from 80 cc. of methyl alcohol, there is obtained 13 g. of crystalline material of the same melting point (Note 2).

2. Notes

1. This crude material dried over night at about 40° is practically pure and if used at once is satisfactory for the preparation of diphenylmethane imine hydrochloride (p. 28).

2. In the presence of oxygen and traces of moisture, benzo-

phenoneoxime is gradually converted into a mixture of benzophenone and nitric acid.[1] A good method of preserving this substance is to dry it in a vacuum desiccator, fill the desiccator with pure carbon dioxide, re-evacuate, and fill again with carbon dioxide. The preparation may then be transferred to a bottle, also filled with carbon dioxide, and sealed against access of air.

3. Methods of Preparation

Benzophenoneoxime has been prepared in quantity by treating an aqueous alcoholic mixture of benzophenone and hydroxylamine hydrochloride with hydrochloric acid,[2] with sodium carbonate,[3] with alcoholic potassium hydroxide,[4] or with aqueous sodium hydroxide.[5] It has also been obtained by treating bisnitrosylbenzohydryl with alcoholic potassium hydroxide,[6] and by the oxidation of α-aminodiphenylmethane with magnesium persulfate solution.[7]

[1] Hollemann, Rec. trav. chim. **13**, 429 (1894); Lachman, J. Am. Chem. Soc. **46**, 1478 (1924).
[2] Beckmann, Ber. **19**, 989 (1886).
[3] Janny, Ber. **15**, 2782 (1882).
[4] Derick and Bowmann, J. Am. Chem. Soc. **35**, 1287 (1913).
[5] Lachman, J. Am. Chem. Soc. **46**, 1477 (1924); **47**, 260 (1925).
[6] Behrend and Platner, Ann. **278**, 369 (1894).
[7] Bamberger and Seligman, Ber. **36**, 704 (1903).

V

BROMOACETONE

$$CH_3COCH_3 + Br_2 \rightarrow CH_3COCH_2Br + HBr$$

Submitted by P. A. LEVENE.
Checked by FRANK C. WHITMORE and J. PAULINE HOLLINGSHEAD.

1. Procedure

A 5-l. three-neck round-bottom flask is provided with an efficient mechanical stirrer, a 48-cm. Allihn reflux condenser, a thermometer, and a 500-cc. separatory funnel, the stem of which reaches nearly to the bottom of the flask (Note 1).

Through the separatory funnel are introduced 1600 cc. of water, 500 cc. of C. P. acetone, and 372 cc. of glacial acetic acid. The stirrer is started and the temperature of the water bath is raised to 70–80°, so that the mixture in the flask is at about 65° (Note 2). Then 354 cc. (7.3 moles) of bromine is carefully added through the separatory funnel. The addition is so regulated as to prevent the accumulation of unreacted bromine (Note 3). The addition requires one to two hours. As a rule the solution is decolorized in about twenty minutes after the bromine has been added. When the solution is decolorized, it is diluted with 800 cc. of cold water, cooled to 10°, made neutral to Congo Red with about 1000 g. of solid anhydrous sodium carbonate, and the oil which separates is collected in a separatory funnel and dried with 80 g. of anhydrous calcium chloride. After drying, the oil is fractionated and the fraction boiling at 38–48°/13 mm. is collected. The yield is 470–480 g. (47–48 per cent of the theoretical amount). It may be used without further purification for the preparation of acetol (p. 1), but if a purer product is desired, the above product is refractionated

and the fraction boiling at 40–42°/13 mm. is collected. The yield is 400–410 g. (40–41 per cent of the theoretical amount).

The higher boiling fraction contains a mixture of isomeric dibromoacetones.

2. Notes

1. The apparatus should be set up with the flask in a large container (such as a 14-qt. galvanized pail) to be used as a water bath, and under a well-ventilated hood, as both the bromine and bromoacetone are powerful irritants to the skin and mucous membranes.

2. It is necessary that the reaction mixture be warmed to this temperature to insure a smooth reaction.

3. It is not advisable to have too great an excess of bromine present at any time, as it sometimes reacts suddenly with great violence.

3. Methods of Preparation

Bromoacetone may be prepared by allowing bromine and acetone to stand with ten times the volume of water, and steam distilling the resulting oil.[1] It may also be prepared by conducting 138 parts of bromine into 100 parts of cold acetone by means of a current of air.[2] Scholl and Matthaiopoulos prepared bromoacetone by introducing 1 part of bromine into 4 parts of acetone in which 1 part of marble was suspended, and gradually pouring into the mixture 2.5 parts of water.[3] Bromoacetone was prepared by Richards by the electrolysis of a mixture of acetone and hydrobromic acid.[4] It has also been prepared by allowing a dilute methyl alcohol solution of chloroacetone and potassium bromide to stand a long time.[5] The method here used is essentially that of Nef.[6]

[1] Sokolowsky, Ber. **9**, 1687 (1876).
[2] Emmerling and Wagner, Ann. **204**, 29 (1880).
[3] Scholl and Matthaiopoulos, Ber. **29**, 1555 (1896).
[4] Richards, Compt. rend. **133**, 879 (1901).
[5] Brendler and Tafel, Ber. **31**, 2683 (1898).
[6] Nef, Ann. **335**, 259 (1904).

VI

α-BROMONAPHTHALENE

$$C_{10}H_8 + Br_2 \rightarrow \alpha\text{-}C_{10}H_7Br + HBr$$

Submitted by H. T. Clarke and M. R. Brethen.
Checked by J. B. Conant and G. W. Wheland.

1. Procedure

In a 1-l. flask are placed 512 g. (4 moles) of naphthalene and 275 g. (170 cc.) of carbon tetrachloride. The flask is equipped with a stirrer, an efficient reflux condenser, and a dropping funnel, the stem of which extends below the level of the liquid. From the top of the reflux condenser a tube leads to a water trap similar to that described in Org. Syn. **8**, 28. The mixture is warmed on the steam bath to gentle boiling, and 707 g. (220 cc., 4.4 moles) of bromine is run in at such a rate that practically none of it is carried over with the hydrogen bromide into the trap. This requires from twelve to fifteen hours, during which time the mixture is gently warmed on the steam bath, with continual stirring, until the evolution of hydrogen bromide ceases (about six hours). The mixture is now distilled from the steam bath under slightly reduced pressure (using a condenser) until free of carbon tetrachloride; the residue is mixed with 20–30 g. of powdered or granulated sodium hydroxide and stirred at 90–100° for four hours (Note 1). The liquid is transferred to a flask for fractional distillation and distilled under reduced pressure. The forerun contains a considerable proportion of unchanged naphthalene, the bulk of which is removed by chilling and filtering with suction; the main fraction, consisting of bromonaphthalene, passes over at 160–165°/15 mm., and a high-boiling fraction (175–185°/15 mm.), consisting of dibromo-

naphthalene, is collected. The intermediate fractions and the filtrates from the foreruns are systematically redistilled; in this way 600–620 g. of colorless α-bromonaphthalene (72–75 per cent of the theoretical amount) and about 30 g. of a mixture of dibromonaphthalenes (m.p., about 60°) are obtained.

2. Notes

1. If this treatment with sodium hydroxide is omitted, the final product contains impurities which gradually give off hydrogen bromide.

3. Methods of Preparation

The above method has been found to be more convenient and to give considerably better yields than that described previously.[1] Bromination of naphthalene in carbon tetrachloride solution has also recently been described by Blicke.[2]

[1] Clarke and Schram, Org. Syn. **1**, 35.
[2] Blicke, J. Am. Chem. Soc. **49**, 2846 (1927).

VII

CASEIN

Submitted by E. J. Cohn and J. L. Hendry.
Checked by H. T. Clarke and W. M. Kennan.

1. Procedure

To one liter of milk, from which the cream has been largely separated (Note 1), 0.05 M hydrochloric acid is slowly added with stirring through a capillary tube extending to the bottom of the beaker. The addition is continued until the solution attains a *p*H of 4.6 (Note 2). The end-point is determined by withdrawing 5-cc. samples, diluting to 50 cc., adding methyl red, and matching against a buffered series (Note 3). Approximately 1000 cc. of acid is required; the separation of the casein is practically complete at this point. Three liters of water is then added, stirring is discontinued, and the flocculent precipitate of casein is allowed to settle in the refrigerator for twelve to twenty-four hours. The clear supernatant liquid which contains soluble proteins and salts is removed as completely as possible by siphoning; the precipitate is collected on a suction funnel and washed with cold distilled water until the washings are free of calcium (give no precipitate with ammonium oxalate).

The casein, which is contaminated with calcium phosphate and fats, is filtered off to as small a volume as possible (about 500 cc.) and transferred to a 2-l. beaker. It is then treated with 0.1 M sodium hydroxide, the alkali being added slowly and with stirring through a capillary extending to the bottom of the beaker (Note 4). The addition of alkali is continued until the *p*H of the mixture reaches 6.3 (Note 5); 100–150 cc. of the alkali is required. The end-point is determined by matching against

a buffered series (Note 6), employing dibromo-*o*-cresolsulfon-phthalein (" bromocresol purple "). At this *p*H the casein is completely in solution in the form of its sodium salt; fats, calcium phosphate and any calcium caseinate remain undissolved. Care must be taken not to add more alkali than is necessary to bring the *p*H to the above point (Note 4). The milky solution is filtered through a thick layer (10–15 mm.) of filter paper pulp tightly packed upon a suction funnel. The filtrate may be slightly opalescent; if it is less clear it is again filtered through a fresh layer of pulp.

The filtrate is brought to a *p*H of 4.6 with 0.05 M hydrochloric acid just as in the original precipitation, the necessary amount of acid being determined by titration of an aliquot portion, diluted five-fold, with 0.01 M hydrochloric acid; 220–250 cc. of 0.05 M acid is required. As the reprecipitation progresses, the rate at which the acid is added is decreased in order to prevent precipitation at the tip of the capillary tube; vigorous mechanical stirring is, of course, essential. When the acidification is complete, 5 l. of cold distilled water is added and the flocculent precipitate allowed to settle in the refrigerator. After siphoning off the clear supernatant liquid, the casein is collected on a suction funnel, using hardened paper, washed with cold distilled water until free of chloride, sucked as dry as possible and dried over calcium chloride in a vacuum desiccator. The yield is 23–29 g. of a colorless coherent product which may readily be pulverized in a mortar.

2. Notes

1. The cream is satisfactorily removed by allowing the milk to stand in a refrigerator over night and siphoning off the lower layer.

2. Casein exists in milk in the form of a calcium derivative; *p*H 4.6 is the isoelectric point of free casein, which is soluble to the extent of only 0.11 g. per liter.[1]

[1] Cohn, J. Gen. Physiol. **4**, 697 (1922).

3. Buffers for this range may be made up as follows:

0.1 M Acetic Acid	0.1 M Sodium Acetate	*p*H
7.35 cc.	2.65 cc.	4.2
6.3	3.7	4.4
5.1	4.9	4.6
4.0	6.0	4.8
2.95	7.05	5.0

4. It is important to avoid a local excess of alkali, which would tend to denature the casein.[2]

5. At this *p*H sodium caseinate is largely dissolved, whereas calcium caseinate is largely undissolved.[3]

6. The buffer series may conveniently be prepared as follows:

Disodium Phosphate (M/15)	Monopotassium Phosphate (M/15)	*p*H
0.78 cc.	9.22 cc.	5.8
1.2	8.8	6.0
1.85	8.15	6.2
2.65	7.35	6.4
3.75	6.25	6.6
5.0	5.0	6.8

3. Methods of Preparation

The precipitation of casein in its uncombined form by the addition to milk of one or another acid, forms the basis of all methods of preparation. These differ widely, however, in the subsequent purification. In the method of Hammarsten,[4] just enough alkali is added to dissolve this casein completely. The alkalinity reached in this process somewhat modifies its physical properties but probably not its composition. In the method of Van Slyke and Bosworth [5] the last trace of calcium is removed by adding oxalate to an ammoniacal solution of the casein, but

[2] Cohn and Hendry, J. Gen. Physiol. **5**, 521 (1923).

[3] Loeb, J. Gen. Physiol. **3**, 547 (1920–21).

[4] Hammarsten, Textbook of Physiological Chemistry, translation of 7th Edition, 619 (John Wiley, 1911).

[5] Van Slyke and Bosworth, J. Biol. Chem. **14**, 211 (1913).

this procedure was shown to be unnecessary by Van Slyke and Baker.[6]

The present process is based in large part upon that of Van Slyke and Baker, the modifications depending upon the observation that casein forms far more soluble compounds with univalent than with bivalent bases at neutral reactions.

[6] Van Slyke and Baker, J. Biol. Chem. **35**, 127 (1918).

VIII

o-CHLOROBENZOIC ACID

$$ClC_6H_4CH_3 + 2KMnO_4 \rightarrow ClC_6H_4COOK + 2MnO_2 + KOH + H_2O$$

Submitted by H. T. CLARKE and E. R. TAYLOR.
Checked by HENRY GILMAN and J. H. MCGLUMPHY.

1. Procedure

IN a 12-l. flask fitted with stirrer and reflux condenser are placed 600 g. (3.8 moles) of potassium permanganate, 7 l. of water and 200 g. (1.6 moles) of *o*-chlorotoluene (Org. Syn. **3**, 33). The mixture is slowly heated to boiling (Note 1) with continual stirring, until the permanganate color has disappeared. This requires three to four hours. The condenser is now set downward for distillation and the mixture is distilled, with constant stirring, until no more oil passes over with the water. The unattacked *o*-chlorotoluene thus obtained amounts to 25–30 g. The hot mixture is filtered with suction and the cake of hydrated manganese dioxide washed with two 500-cc. portions of hot water. The combined filtrate is concentrated (Note 2) to about 3.5 l.; if it is not entirely clear it may be clarified by the use of 1–2 g. of decolorizing carbon. It is now, while still hot, acidified by cautiously adding 250 cc. of concentrated hydrochloric acid (sp. gr. 1.19) with continual agitation. When the mixture is cool the white precipitate of *o*-chlorobenzoic acid is filtered off and washed with cold water. The dry weight is 163–167 g. (74–78 per cent of the theoretical amount, based on the amount of *o*-chlorotoluene actually oxidized) of a very nearly pure (Note 3) product melting at 137–138°. For purification this may be recrystallized from 600 cc. of toluene, when 135–140 g. of a product melting at 139–140° is obtained. Further crops can be obtained by concentrating the mother liquor.

2. Notes

1. If the mixture is heated too rapidly the reaction may be violent at the outset. In such a case it can be controlled by laying wet towels upon the upper part of the flask.

2. This concentration is satisfactorily carried out on the steam bath under reduced pressure (Org. Syn. 4, 54).

3. Care must be taken to use pure *o*-chlorotoluene in this preparation; otherwise the *o*-chlorobenzoic acid may be contaminated with isomeric acids which are very difficult to remove. The *o*-chlorotoluene therefore should be prepared from pure *o*-toluidine or *o*-chlorotoluenesulfonic acid.

3. Methods of Preparation

The only practical methods of preparing *o*-chlorobenzoic acid consist in the oxidation of *o*-chlorotoluene and the replacement of the amino group in anthranilic acid by a chlorine atom. Both of these methods have been fully discussed by Graebe,[1] who recommends the former for the preparation of relatively large quantities. The oxidation of *o*-chlorotoluene by permanganate was originally described by Emmerling.[2]

[1] Graebe, Ann. **276**, 54 (1893).
[2] Emmerling, Ber. 8, 880 (1875).

IX

DIMETHYLGLYOXIME

$$C_2H_5OH + HNO_2(NaNO_2 + H_2SO_4) \rightarrow C_2H_5ONO + H_2O$$

$$C_2H_5ONO + CH_3COCH_2CH_3 \rightarrow CH_3COC{=}(NOH)CH_3 + C_2H_5OH$$

$$\begin{array}{l} CH_3C{=}O \\ \quad | \\ CH_3C{=}NOH \end{array} + NaO_3SNHOH \rightarrow \begin{array}{l} CH_3C{=}NOH \\ \quad | \\ CH_3C{=}NOH \end{array} + NaHSO_4$$

Submitted by W. L. Semon and V. R. Damerell.
Checked by Henry Gilman and R. E. Fothergill.

1. Procedure

A. Ethyl Nitrite.—Two solutions are prepared. Solution I contains 620 g. (9 moles) of sodium nitrite (650 g. of technical 95 per cent), 210 g. (4.57 moles) of alcohol (285 cc. of 90 per cent denatured, or its equivalent) and water to make a total volume of 2500 cc. Solution II contains 440 g. of sulfuric acid (255 cc. of sp. gr. 1.84) and 210 g. of alcohol, diluted with water to 2500 cc. Ethyl nitrite may be generated continuously in gaseous form by allowing solution II to flow into solution I.

The gas can be conveniently made by putting solution II in a 2.5-l. bottle fitted with a two-hole rubber stopper (Fig. 1) and provided with glass tubing as indicated in the diagram. The rate of flow of solution II into a 6-l. bottle containing solution I is regulated by a screw clamp. The ethyl nitrite generated flows out of the second opening in the stopper of the lower bottle. The stoppers to both bottles should be wired on. A mechanical stirrer in the lower bottle is helpful in securing a steady evolution of the gas (Note 1).

B. Biacetyl Monoxime.—In a 2-l. three-neck flask provided with a condenser, a thermometer and an inlet tube for ethyl

nitrite, and arranged for external cooling, is placed 620 g. (775 cc.) of commercial methyl ethyl ketone which has been dried with, and filtered from, 75 g. of anhydrous copper sulfate. Forty cc. of hydrochloric acid (sp. gr. 1.19) is added (Note 2) and the temperature raised to 40°. The ethyl nitrite from the preceding preparation is now bubbled in, the temperature being maintained between 40 and 55°. After all of the ethyl nitrite has been passed in (Note 3) the crude product may be used in the preparation of dimethylglyoxime by distilling off the alcohol formed in the reaction until the temperature of the liquid reaches 90° (Note 4).

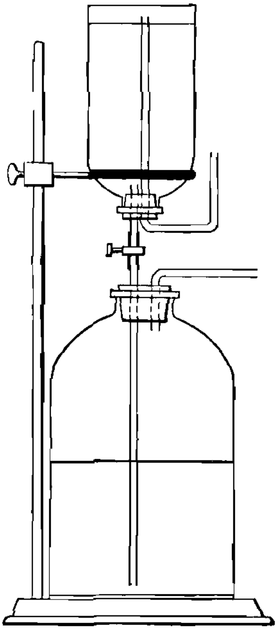


FIG. 1.

If pure biacetyl monoxime is desired, the crude product is neutralized with about 35 cc. of concentrated aqueous ammonia and diluted with half its volume of water. It is then distilled to remove alcohol, etc., until the distillate is no longer inflammable. The receiver is changed and the contents are now rapidly distilled, using superheated steam. Almost all of the biacetyl monoxime comes over in the first 5 l. of distillate. One to 1.5 kg. of salt is dissolved in the distillate, which is then cooled to 0°. The solid biacetyl monoxime crystallizes out and may be filtered off. The yield is 480–520 g. The product can be further purified, if desired, by recrystallizing from water (Note 5).

C. Sodium Hydroxylamine Monosulfonate.—In a 12-l. crock are mixed 5 kg. of shaved ice (Note 6) and 569 g. of sodium nitrite (594 g. of the technical 95 per cent quality). Into this is stirred a suspension of sodium bisulfite containing 1100 g. of available sulfur dioxide (about 1775 g. of technical bisulfite) in 750 cc. of water. Then, beneath the surface of the solution is added, with constant stirring, 150 cc. of glacial acetic acid

(Note 7) followed by a mixture of 550 cc. of concentrated hydrochloric acid (sp. gr. 1.19) with 400 g. of shaved ice (Note 8). The entire solution should always remain below 0°, further ice being added if there is a tendency for the temperature to rise. The solution should now become acid to Congo Red paper and contain 6 or more moles of the sodium hydroxylamine disulfonate, which rapidly hydrolyzes to an acid solution of the monosulfonate.

D. Dimethylglyoxime.—The crude biacetyl monoxime, remaining after distilling to 90° and containing about 5 moles of biacetyl monoxime, is added to the sodium hydroxylamine monosulfonate solution (which has been filtered to remove any sediment) and which is contained in a 15-l. flask. It is heated to 70° and allowed to remain warm (with occasional stirring) for several hours (Note 9). The dimethylglyoxime separates in crystals which can be filtered from the solution as soon as it has become cold (Note 10). The crystals are washed with cold water until free of sulfate. The yield of compound melting at 238–240° is 540–575 g.

Recrystallization is unnecessary since the product is pure white and free from tarry material (Note 5).

E. Sodium Dimethylglyoximate.—To a solution of 75 g. of sodium hydroxide in 300 cc. of water is added, with stirring, 100 g. of dimethylglyoxime (Note 11). Heat is applied to effect solution (Note 12), and the mixture is filtered from any slight residue. The solution is poured while hot into 500 cc. of 95 per cent alcohol. After cooling to 5°, with stirring, the crystals which form are filtered, then suspended in 150 cc. of alcohol and again filtered, and finally dried at 25° until the solid has no odor of alcohol (Note 13). The yield is 213–230 g. (81–88 per cent of the theoretical amount) of the octahydrate.

2. Notes

1. If a mechanical stirrer is not used care should be exercised to prevent a layer of solution II from collecting at the bottom of solution I, since under these conditions a little shaking produces too violent an evolution of gas.

Because ethyl nitrite is harmful if inhaled continuously, the reaction should be carried out in a hood or out of doors.

2. The methyl ethyl ketone should not be allowed to stand any length of time between the addition of the hydrochloric acid and the treatment with ethyl nitrite, inasmuch as the acid causes a condensation of the ketone with itself, thereby lowering the yield of biacetyl monoxime.

3. The ethyl nitrite may be passed into the solution as rapidly as possible, providing the temperature does not exceed 55°. Very complete absorption takes place, and the time of addition is about one and one-half hours.

4. Care should be taken that the distillation for the removal of alcohol and excess methyl ethyl ketone does not stop under 90° or go beyond this temperature. If stopped too soon, the alcohol that is not boiled off later increases the solubility of the dimethylglyoxime; and too high a temperature causes the formation of tarry products. Both of these factors reduce the yield.

5. About 70–80 per cent of the biacetyl monoxime is recovered on crystallization. Practically all of the monoxime left in the mother liquor can be recovered by steam distillation. The recrystallized and dried compound melts at 76.5°. Purification by distillation is not recommended.

The biacetyl monoxime turns brown rapidly after preparation and it must not be allowed to stand before adding it to the hydroxylamine monosulfonate in the preparation of dimethylglyoxime if this final product is to be obtained in a colorless condition.

6. Shaved ice is used in place of crushed ice because of more efficient cooling. The use of snow is advised, if it is available.

7. The acetic acid helps to buffer the solution and maintain a low hydrogen-ion concentration, which is favorable for a good yield.

8. The acid may be added as rapidly as desired so long as the temperature remains below 0° and no evolution of gas takes place. The entire addition should require not more than fifteen minutes.

9. The mixture is warmed to hasten the hydrolysis of disulfonate to monosulfonate, and also to increase the solubility of the biacetyl monoxime in the monosulfonate solution.

10. The dimethylglyoxime should not be filtered off until the mixture has become perfectly cool, because dimethylglyoxime is slightly soluble in a warm acid solution.

11. Crude or discolored dimethylglyoxime may be used since the impurities remain in solution in the aqueous alcohol.

12. The solution of dimethylglyoxime in sodium hydroxide should not be boiled, since prolonged heating causes decomposition.

13. The sodium salt may be further purified if desired by dissolving in water and reprecipitating with alcohol. Large crystals may be secured by crystallizing slowly from water.

Too long drying, or drying at too high a temperature, partially dehydrates the salt, with the result that it dissolves much more slowly in water and is therefore less desirable for making solutions for use in qualitative or quantitative analysis. Sodium dimethylglyoximate is extremely soluble in water. A 3 per cent (0.1 M) aqueous solution is suggested to replace the 1 per cent alcoholic solution now used in analytical work.

3. Methods of Preparation

Biacetyl monoxime has been prepared by the action of amyl nitrite on methyl ethyl ketone using sodium hydroxide [1] or hydrochloric acid [2] as a condensing agent, and by melting nitrosolevulinic acid.[3]

Dimethylglyoxime has been prepared by the action of hydrochloric acid upon biacetyl monoxime; [4] by the action of hydroxylamine on biacetyl; [5] by the action of hydroxylamine on biacetyl

[1] Claisen, Ber. **38**, 696 (1905).

[2] Diels and Farkas, Ber. **43**, 1957 (1910); Biltz, Z. anal. Chem. **48**, 164 (1909); Semon and Damerell, J. Am. Chem. Soc. **47**, 2038 (1925).

[3] Thal, Ber. **25**, 1720 (1892).

[4] Schramm, Ber. **16**, 180 (1883); Johlin, J. Am. Chem. Soc. **36**, 1218 (1914).

[5] Fittig, Daimler, and Keller, Ann. **249**, 182 (1888); Wolff, Ann. **288**, 1 (1895).

monoxime;[6] and by the action of sodium hydroxylamine monosulfonate on biacetyl monoxime.[7] It is formed in small amounts, together with ethylnitrolic acid, by the action of oxides of nitrogen upon methyl ethyl ketone.[8]

[6] Tschugaeff, Ber. **38**, 2520 (1905); Gandarin, *J. prakt. Chem.* (2) **77**, 414 (1908); Biltz, Z. anal. Chem. **48**, 164 (1909); Adams and Kamm, *J.* Am. Chem. Soc. **40**, 1281 (1918).

[7] Semon and Damerell, J. Am. Chem. Soc. **46**, 1290 (1924); **47**, 2033 (1925).

[8] Behrend and Tryller, Ann. **283**, 244 (1894).

X

DIPHENYLMETHANE IMINE HYDROCHLORIDE

$$8(C_6H_5)_2C{=}NOH \rightarrow$$
$$4(C_6H_5)_2CO + 4(C_6H_5)_2C{=}NH + N_2 + 2H_2O + 2NO$$
$$(C_6H_5)_2C{=}NH + HCl \rightarrow (C_6H_5)_2C{=}NH \cdot HCl$$

Submitted by Arthur Lachman.
Checked by C. R. Noller.

1. Procedure

A piece of glass tubing 80 cm. long and 2 cm. in internal diameter is sealed at one end and loosely packed with 49 g. (0.25 mole) of benzophenoneoxime (p. 10). The tube is supported in a nearly horizontal position, dipping slightly toward the closed end, and connected to a small filter flask by means of rubber stoppers and a piece of glass tubing bent at a right angle. The system is evacuated by means of a water pump and dry carbon dioxide admitted, re-evacuated, and carbon dioxide admitted again. The oxime is then heated with a free flame beginning at the upper end and heating at one spot until decomposition takes place before heating a further portion (Note 1). When all of the oxime has been decomposed, the mixture which has collected at the closed end of the tube (Note 2) is heated strongly for a short time to complete the decomposition, and allowed to cool. Suction is again applied to the tube and the condensed water is driven out by gently warming the tube. The liquid is then transferred to a small distilling flask and distilled at a pressure of about 20 mm. The distillate, consisting of a mixture of benzophenone and diphenylmethane imine, is dissolved in 400 cc. of ligroin (60–90°) and the imine hydrochloride is precipitated by bubbling in dry hydrogen chloride. The salt is filtered with suction (Note 3), washed with a little ligroin, dried, and pre-

served in a dry atmosphere (Note 4). It sublimes without decomposition at 230–250° (Note 5). The yield is 16–18 g. (59–66 per cent of the theoretical amount) (Note 6).

2. Notes

1. When the heating is carefully done, no material is carried out of the tube with the gases.

2. Care should be taken to prevent any drops of water that have condensed in the cool portion of the tube from running back and mixing with the liquid that is being heated.

3. Benzophenone may be recovered from the filtrate.

4. In moist air the hydrochloride is changed to a mixture of benzophenone and ammonium chloride. The free base on standing in air gives off ammonia and gradually deposits crystals of benzophenone.

5. The imine salt can be converted into the free base by the method of Hantzsch and Kraft, which involves treating a solution of the salt in chloroform with dry ammonia.

6. The yield depends greatly on the quality of the benzophenoneoxime. If this contains moisture or has been exposed to moist air, especially in a closed space, for any length of time, the yield is markedly decreased.

3. Methods of Preparation

Diphenylmethane imine (or its hydrochloride) has been obtained by heating diphenyldichloromethane with urethane at 130°;[1] by the action of ammonia on diphenyldibromomethane;[2] by treating benzophenonechloroimide with phosphorus pentachloride in ether solution,[3] or dry hydrogen chloride in ligroin solution;[4] by the action of phenylmagnesium bromide on *N*-bromobenzamide,[2] benzonitrile,[5] cyanogen bromide,[6] cyano-

[1] Hantzsch and Kraft, Ber. **24**, 3516 (1891).

[2] Moore, Ber. **43**, 564 (1910).

[3] Vosburgh, J. Am. Chem. Soc. **38**, 2095 (1916).

[4] Peterson, Am. Chem. J. **46**, 331 (1911).

[5] Moureu and Mignonac, Compt. rend. **156**, 1806 (1913); Ann. Chim. (9) **14**, 336 (1920).

[6] Grignard, Bellet and Courtot, Ann. chim. (9) **4**, 34 (1915).

gen chloride,[7] and alkyl thiocyanates.[8] It has also been obtained by passing a mixture of ammonia and benzophenone vapor over thorium oxide at 380–390°;[9] by the catalytic reduction of benzophenoneoxime using hydrogen and a nickel catalyst in absolute alcohol solution at ordinary temperature and pressure;[10] by passing a mixture of hydrogen and benzophenoneoxime vapor over reduced copper at 200°;[11] and by the action of sodium ethylate on *N*-monochlorodiphenylmethylamine in alcoholic solution.[12] The method described here has been previously published by Lachman.[13]

[7] Grignard, Bellet and Courtot, Ann. chim. (9) **12**, 379 (1919).
[8] Adams, Bramlet and Tendick, J. Am. Chem. Soc. **42**, 2372 (1920).
[9] Mignonac, Compt. rend. **169**, 239 (1919).
[10] Mignonac, Compt. rend. **170**, 938 (1920).
[11] Yamaguchi, Bull. Chem. Soc. Japan **1**, 35 (1926) [C. A. **21**, 75 (1926)].
[12] Hellerman and Sanders, J. Am. Chem. Soc. **49**, 1742 (1927).
[13] Lachman, J. Am. Chem. Soc. **46**, 1477 (1924).

XI

DURENE

(1,2,4,5-*Tetramethyl benzene*)

(By-products, Penta- and Hexa-methyl benzenes)

$$C_6H_4(CH_3)_2 + 2CH_3Cl \xrightarrow{AlCl_3} C_6H_2(CH_3)_4(1,2,4,5) + 2HCl$$

Submitted by LEE IRVIN SMITH.
Checked by F. C. WHITMORE and THOS. E. HOLLINGSHEAD.

1. Procedure

A 5-l. flask, mounted on a steam bath, is fitted with a wide (Note 1) inlet tube reaching to the bottom of the flask, a reflux condenser, and a delivery tube running from the top of the reflux condenser and reaching to the bottom of a heavy glass cylinder containing a column of mercury about 10 cm. high. All stoppers and joints of the apparatus must fit tightly and be wired, as the reaction is carried out under a slight pressure. In the flask are placed 3180 g. (3700 cc., 30 moles) of xylene (Note 2) and 1000 g. of anhydrous aluminium chloride (Note 2). The inlet tube of the flask is then connected to a tank of methyl chloride or to a methyl chloride generator (Note 3), the steam is turned on in the bath, and a fairly rapid stream of methyl chloride is passed into the mixture (Note 4). At first there will be a rapid absorption, and the stream of gas must be regulated so that the mercury in the pressure tube does not tend to suck back. The hydrogen chloride formed may be conveniently disposed of by a trap devised by Johnson (Org. Syn. 8, 27, Note 2). As the reaction slows down, the pressure increases until both hydrogen chloride and methyl chloride begin to escape through the mer-

cury. At this point the current of incoming gas should be cut down so that undue loss of methyl chloride is avoided. About one hundred hours are required for the completion of the reaction (Note 5).

When the reaction is completed, the steam is turned off and the flask is disconnected and loosely stoppered. After standing over night the reaction mixture is decomposed by pouring it slowly into 5 kg. of chopped ice. The greenish oil which separates from the aqueous layer is removed, dried over calcium chloride, filtered and fractionated twice, using a round-bottom flask fitted with an efficient column and an air condenser (Note 6).

The fractions are cut as follows:

Fraction	Temp. Range	Distillate	Yield, g.
I and II	Up to 150°	Benzene, xylene	little
III	150 to 180	Trimethyl benzenes	570
IV	180 to 205	Tetramethyl benzenes	2075
V	Above 205	Mostly pentamethyl benzene	815

Typical yields of the various fractions are given in the table; they may vary 10 to 20 per cent from these figures, owing to slight differences in procedure and materials, and especially to differences in the quality of the aluminium chloride employed. The more efficient this material is, the greater the percentage of the higher boiling fractions.

The tetramethyl benzene fraction (IV) is rich in durene, which may be frozen out and filtered off because of its relatively high melting point (80°). To isolate the durene, fraction IV is thoroughly chilled in an ice-calcium chloride pack, and filtered off through a cold filter (Note 7) using good suction, and pressing down the solid compactly. When no more liquid drips through the cold filter, the filtration apparatus is allowed to come gradually to room temperature (Note 7) and the suction is continued as long as any liquid drips through, after which the solid is removed and bottled. The yield is 540 to 610 g.

Fraction III may be methylated to the tetramethyl benzene stage by heating on the steam bath with 100 g. of anhydrous aluminium chloride and passing in 225 g. of methyl chloride. The filtrates from the durene likewise yield more durene when heated

on the steam bath with 50 g. of aluminium chloride. The products are worked up in the usual way, that is, they are decomposed by pouring into twice their weight of chopped ice, separated from the aqueous layer, fractionated twice, and the durene frozen out as before. By conducting one methylation of the trimethyl benzene fraction, and one treatment of the durene filtrates, the combined yield of crude durene will average 1000 to 1400 g. (25–35 per cent of the theoretical amount based on the original 30 moles of xylene).

To purify the durene, 200 g. of the crude product is placed in a 1-l. round-bottom flask fitted with a reflux condenser, and melted in a water bath at 95°; 200 cc. of warm (50°) 95 per cent ethyl alcohol is then added through the top of the condenser, and the mixture is carefully heated until homogeneous. The solution is filtered on a hot-water funnel, allowed to stand tightly covered (Note 8) in a fairly warm place (35°) over night, cooled to about 0°, and filtered on a suction filter. The product (about 169 g.) melts at 74–78°. A second recrystallization yields 149 g. melting at 77–79°. A third recrystallization yields 140 g., having a melting point of 79–80°. The alcoholic filtrates are fractionated and the crude durene obtained is worked over with the isomers of durene.

Pentamethyl benzene.—Fraction V, and xylene which is methylated beyond the tetramethyl benzene stage, may be worked up for pentamethyl benzene. If xylene is to be methylated to obtain pentamethyl benzene, one more mole of methyl chloride should be used, and the mixture of xylene and anhydrous aluminium chloride methylated for one hundred and ten hours instead of the one hundred used for durene. Otherwise the procedure is exactly the same as for durene. The reaction mixture is decomposed and fractionated in the usual way, and the material boiling above 205° (fraction V) is separated into three fractions:

Fraction	Temperature Range	
VI	205–215°	Tetra- and pentamethyl benzene
VII	215–235	Mostly pentamethyl benzene
VIII	Residue above 235	Hexamethyl benzene and tars

The pentamethyl benzene obtained in this way is nearly pure, and one recrystallization from 95 per cent alcohol or from a mixture of equal volumes of alcohol and benzene gives a snow-white product, but the product generally melts over too wide a range for practical purposes. However, if fraction VII is refractionated under diminished pressure and the fraction boiling at 123–133°/22 mm. (practically all at 127–129°) is collected and recrystallized as in the following paragraph, a product melting quite sharply at 52° (true m.p. 53°) is obtained.

Six hundred grams of crude pentamethyl benzene is heated to 100° and poured slowly with stirring into 1000 cc. of 95 per cent ethyl alcohol heated to 70° in a 2-l. beaker, and allowed to stand over night at a temperature of approximately 30°. The crystals formed are collected on a suction filter and dried at room temperature over night on a porous plate. The yield is about 250 g. (Note 9).

Hexamethyl benzene.—Fraction VIII is fractionated in 250-cc. batches in a Claisen flask at 20 mm. pressure, the following fractions being collected:

Fraction	Temperature Range	
IX	80–110°	Mostly tetra- and pentamethyl benzenes
X	110–135	Mostly pentamethyl benzene
XI	135–170	Hexamethyl benzene
XII	Residue above 170	Hexamethyl benzene and tars

This fractionation may be carried out in an ordinary Claisen flask, but there is some difficulty in maintaining the desired pressure due to the solvent action of the hydrocarbons on the rubber stopper. This difficulty may be avoided by the use of a Claisen flask with very long necks and a wide side-tube. The material should be distilled fast enough to prevent it from solidifying in the column and side tube. Prolonged heating of hexamethyl benzene also causes a considerable amount of decomposition to tars.

The method for the production of large amounts of hexamethyl benzene is the rapid methylation of pentamethyl benzene or the durene filtrates. A mixture of 378 g. of pentamethyl benzene and 200 g. of anhydrous aluminium chloride is heated

on an oil bath at 190–200° and a rapid stream of dry methyl chloride is bubbled through for three to four hours, using the same apparatus as was used for the preparation of durene. The mixture is allowed to stand over night at room temperature. One liter of hot xylene is added to dissolve the solidified material, and the reaction mixture is decomposed by pouring it onto 3 kg. of chopped ice. The resulting oil is separated and the xylene and other low boiling material is removed by distillation under reduced pressure (Note 10). The fractions are divided as above. Two refractionations and two recrystallizations (Note 11) give 98–121 g. of white crystals, melting at 157–161° (Note 12).

2. Notes

1. The inner tube of a condenser makes a good inlet tube. It should be placed so that the wide end is inside the large flask.

2. The xylene should be a good, colorless laboratory grade, b.p. 135–140°. Any moisture present may be removed by distilling and discarding the first 10 per cent of the distillate. The best aluminium chloride available should be used, for the methylation is very unsatisfactory if the catalyst is of an inferior grade. It should be in small pieces, but need not be powdered.

3. The methyl chloride generator consists of a 5-l. flask resting on a sand bath and fitted with a reflux condenser, with a delivery tube running from the top of the condenser to a train of wash bottles, two containing water and two containing concentrated sulfuric acid, with three safety bottles, one at each end of the train, and one between the water and sulfuric acid bottles. To charge for about 45 moles (theoretical) of methyl chloride: 200 g. of water and 2200 g. (1200 cc.) of concentrated sulfuric acid are placed in the flask, and 1400 g. (1760 cc.) of methyl alcohol is added, with cooling, at such a rate that the temperature does not rise above 70°. Then 2400 g. of sodium chloride is added, the apparatus is tightly connected, and the flask heated on the sand bath so that the gas is evolved at a fairly rapid rate. It has been found in practice that, using materials of the commercial grade, the yield of methyl chloride is about 55 to 65 per

cent of the theoretical amount, so that about double the calculated quantities must be used. This means that the generator has to be charged three times in order to convert 30 moles of xylene to tetramethyl benzene. If a tank of methyl chloride is available, 65–70 moles of methyl chloride should be used for this same amount of xylene. The tank should be weighed before starting and the reaction stopped when the tank has lost the proper amount in weight.

4. Experiments have shown that the rapid current of methyl chloride furnishes sufficient stirring.

5. The normal time of one hundred hours can be shortened by increasing the amount of aluminium chloride. The product in this case, however, is very viscous and rather difficult to handle in large amounts.

6. Two systematic fractionations (not redistillations) with a good column are absolutely necessary in order to obtain good separations. The more efficient the column the better.

7. The material should be filtered through a large Büchner funnel, which is immersed in a freezing mixture as long as any liquid drips through. It is stated in the literature that the first filtrate obtained in this way is mostly isodurene (1,2,3,5-), whereas the second filtrate, obtained as the material warms slowly to room temperature, is pseudodurene or prehnitene (1,2,3,4-), m.p. -4°.

8. Durene is quite volatile, and should not be allowed to remain exposed to the air any longer than necessary. It is also quite volatile with alcohol, and the mother liquors resulting from the recrystallizations should be distilled: the alcoholic distillate is used for further recrystallizations, and the residues may be worked up for durene by heating with aluminium chloride.

9. The melting point of pentamethyl benzene is only slightly affected by recrystallization, because most of the impurity is hexamethyl benzene, which can be removed only by fractionation.

10. Hexamethyl benzene decomposes when heated very strongly for any length of time. Better results are therefore obtained if the distillations are carried out under reduced pressure.

11. Small amounts of impurities greatly influence the melting point of hexamethyl benzene, and several recrystallizations of a fraction of close boiling range are necessary in order to prepare a sharply melting product.

12. Small amounts (25 g. or less) of hexamethyl benzene which is nearly pure, are best recrystallized from ethyl alcohol. It requires about 600 cc. of boiling alcohol to dissolve 25 g., but on cooling 20 g. of pure product will result. Ether and benzene dissolve the substance much more readily, and larger amounts of materials are best recrystallized from either of these solvents, or from a mixture of one of them with alcohol. 125 g. of the hexamethyl benzene distillate which has been refractionated is melted and poured slowly with stirring into 1500 cc. of 95 per cent alcohol. A small amount remains undissolved and may be brought into solution by adding about 300 cc. of hot benzene, the beaker being heated on a steam bath and the mixture stirred constantly until all is dissolved. The solution is allowed to stand over night at approximately 25°. The crystals are filtered off by suction and washed with enough 95 per cent alcohol to moisten thoroughly (about 25 cc.). After drying, the crystals weigh approximately 112 g. and melt at 155–159°.

3. Methods of Preparation

Durene, pentamethyl benzene and hexamethyl benzene have usually been prepared from benzene or one of its methylated derivatives by the Friedel-Crafts synthesis.[1] Durene has been made from bromine derivatives of methylated benzenes by the Fittig reaction.[2] It has also been obtained in 20 per cent yield by passing methyl alcohol and acetone vapors over heated alu-

[1] Ador and Rilliet, Ber. **12**, 331 (1879); Friedel and Crafts, Compt. rend. **91**, 257 (1880); Ann. chim. phys. (6) **1**, 449 (1884); Jacobsen, Ber. **14**, 2629 (1881); **18**, 338 (1885); **20**, 896 (1887); Anschütz, Ann. **235**, 185 (1886); Claus and Foecking, Ber. **20**, 3097 (1887); Beaurepaire, Bull. soc. chim. **50**, 676 (1888).

[2] Jannasch and Fittig, Z. Chem. **13**, 161 (1870); Jannasch, Ber. **7**, 692 (1874); **10**, 1354 (1877).

minium oxide.[3] Hexamethyl benzene has been obtained by the action of zinc chloride on methyl alcohol [4] or on acetone.[5] The method given in the procedure has recently been described in the literature.[6]

[3] Reckleben and Scheiber, Ber. **46**, 2363 (1913).
[4] LeBel and Greene, Compt. rend. **87**, 260 (1878).
[5] Greene, Compt. rend. **87**, 931 (1878).
[6] Smith and Dobrovolny, J. Am. Chem. Soc. **48**, 1413 (1926).

XII

DUROQUINONE

$$C_6H_2(CH_3)_4(1,2,4,5) \rightarrow C_6(CH_3)_4(NO_2)_2$$

$$2C_6(CH_3)_4(NO_2)_2 \xrightarrow{SnCl_2 + HCl} [C_6(CH_3)_4(NH_2 \cdot HCl)_2]_2 \cdot SnCl_4$$

$$[C_6(CH_3)_4(NH_2 \cdot HCl)_2]_2 \cdot SnCl_4 \xrightarrow{FeCl_3} 2C_6(CH_3)_4O_2$$

Submitted by LEE IRVIN SMITH.
Checked by F. C. WHITMORE and THOS. E. HOLLINGSHEAD.

1. Procedure

A. Dinitrodurene.—A solution of 13.4 g. (0.1 mole) (Notes 1,2) of durene (p. 32) in 100 cc. of chloroform is added to 75 cc. of concentrated sulfuric acid in an 800-cc. beaker provided with a thermometer and an efficient mechanical stirrer. The mixture is cooled to 10°, and 16 g. (10.7 cc.) of fuming nitric acid (sp. gr. 1.5) (Note 3) is added drop by drop, with stirring, from a 125-cc. separatory funnel, the mixture being cooled in an ice-salt bath and the nitric acid added at such a rate that the temperature does not rise above 50° (about fifteen minutes is required for the addition). As soon as all the acid has been added the mixture is poured into a separatory funnel, the sulfuric acid layer is removed and the upper chloroform layer is immediately (Note 4) run into 500 cc. of 10 per cent sodium carbonate solution. The sulfuric acid layer is discarded because it contains very little dinitrodurene. Four portions are nitrated and the combined chloroform solutions are washed twice with 2.5 per cent sodium carbonate solution, dried over night with 30 g. of anhydrous calcium chloride, filtered, and the chloroform distilled off until crystals of dinitrodurene begin to appear. At this point four times the volume of hot 95 per cent ethyl alcohol is added (about

500 cc.), and the resulting mixture is cooled to 10°. The solid is filtered and washed twice with 50 cc. of cold (10°) 95 per cent ethyl alcohol. The yield from four nitrations is 82.5–84 g. (92–94 per cent of the theoretical amount) of a product melting at 207–208°.

B. Reduction of Dinitrodurene.—A solution of 90 g. of dinitrodurene in 1 l. of glacial acetic acid is boiled in a 12-l. flask (Note 6); 700 g. of stannous chloride is dissolved in 800 cc. of concentrated hydrochloric acid and heated to boiling. The heat is removed from the acetic acid solution of the nitro compound, and the stannous chloride solution is poured very carefully (during about ten minutes) into the dinitrodurene solution. The reaction is complete in fifteen minutes, and as the solution cools the stannic chloride compound of the diamine begins to crystallize. The reaction mixture is cooled to 10° in an ice-water bath, and the solid is filtered off by suction, washed twice with 50 cc. of 95 per cent ethyl alcohol and twice with 50 cc. of ether, and dried. The filtrates from the tin compound contain very little of the reduction product and may be discarded. The composition of this compound is $[C_6(CH_3)_4(NH_2 \cdot HCl)_2]_2 \cdot SnCl_4$, and it crystallizes from the reaction mixture in fine, glistening plates which are almost colorless. The yield is 145 g. (97 per cent of the theoretical amount).

C. Duroquinone.—A suspension of 100 g. of the tin compound in a solution of 300 g. of ferric chloride crystals in a mixture of 150 cc. of water and 20 cc. of concentrated hydrochloric acid is allowed to stand over night at about 30°, and is then filtered. The product is dissolved in 150 cc. of hot 95 per cent ethyl alcohol. The solution is filtered and allowed to stand over night at 30°. The yield is 40 g. of duroquinone (90 per cent of the theoretical amount) melting at 109–110°.

2. Notes

1. It is better to nitrate the durene in small batches, for a high yield and pure product depend upon not allowing the reaction mixture to remain in contact with the nitric acid very long.

2. Pure durene is absolutely essential for good results. It should be recrystallized from methyl alcohol until the melting point is 79–80°.

3. A large excess of nitric acid is undesirable, since it lowers the yield. The concentration of the nitric acid is also of importance, and to obtain the best results, it should have a specific gravity of 1.5 or more.

4. It is important that the chloroform layer be run into the carbonate solution as quickly as possible, for continued standing while in contact with even small amounts of acid leads to the formation of considerable amounts of red, tarry material. This renders the subsequent purification of the nitro compound much more difficult.

5. No mononitrodurene is ever obtained in this process. Either the dinitro compound results, or else unchanged material and oxidation products.

6. A large flask is necessary because the reduction is vigorous and the reaction mixture will boil up and practically fill the flask of the size recommended.

3. Methods of Preparation

Duroquinone, tetramethyl-*p*-benzoquinone, has been prepared in three ways: by the condensation of 2, 3-diketopentane with itself in the presence of alkalies,[1] by the action of alkalies on 3,3-dichloropentanone-2,[2] by means of the series of reactions used in these directions,[3] which is due originally to Nef.[4] The method of nitration used in preparing dinitrodurene according to these directions is a modification of a method of nitration first used by Willstätter.[5]

[1] von Pechmann, Ber. **21**, 1420 (1888).
[2] Faworsky, J. prakt. Chem. (2) **51**, 538 (1895).
[3] Smith and Dobrovolny, J. Am. Chem. Soc. **48**, 1420 (1926).
[4] Nef, Ber. **18**, 2806 (1885); Ann. **237**, 5 (1887).
[5] Willstätter, Ber. **42**, 4151 (1909).

XIII

ERUCIC ACID

$CH_3(CH_2)_7CH{=}CH(CH_2)_{11}CO_2H$

(Hydrolysis of Rape Seed Oil)

Submitted by C. R. NOLLER and R. H. TALBOT.
Checked by H. T. CLARKE and E. R. TAYLOR.

1. Procedure

IN a 5-l. flask fitted with a reflux condenser are placed 2500 cc. of 95 per cent ethyl alcohol and 340 g. (4.5 moles) of commercial (73–75 per cent) potassium hydroxide. The mixture is gently shaken until the hydroxide is dissolved, 1330 g. (1500 cc., approximately 4 equivalents) of rape seed oil is added with shaking (Note 1) and the mixture is refluxed on a steam bath for twenty-five to thirty hours.

The hot mixture is poured, with stirring, into 15 l. of warm water (50–60°), and is followed by 700 cc. (8.2 moles) of concentrated (36 per cent) hydrochloric acid (Note 2). After standing until the layers are distinct (ten to fifteen minutes), the lower layer is siphoned off as completely as possible and the oil is washed with two 1-l. portions of warm water.

The oil thus obtained, which should amount to 1460–1600 cc., is dissolved in three times its volume of 95 per cent ethyl alcohol and the mixture cooled to −10 to 0°, when the erucic acid crystallizes (Note 3). After six to eight hours at this temperature, the crude erucic acid is collected on a basket centrifuge (Note 4). The mother liquor, on chilling, yields a second crop of erucic acid. The combined product (800–1100 g.) melts either partially or wholly at room temperature, owing to the presence of oleic acid. It is dissolved in an equal volume of alcohol,

chilled for six hours at 0°, and centrifuged as before, when it is obtained in well-defined crystalline form. The second crop of this recrystallization resembles that of the first crystallization and must again be recrystallized. The product is finally recrystallized once again from an equal volume of 95 per cent alcohol. The recrystallized acid contains alcohol, which is removed by heating to constant weight on the steam bath under diminished pressure. The yield (Note 5) of acid obtained is 260–360 g.; it melts at 31–32° (Note 6).

2. Notes

1. If the solution is mixed in this manner, the rape seed oil emulsifies on being poured into the alkali and refluxing begins more smoothly.

2. If the acid is added before the water, esterification occurs to an appreciable extent, so that the yield may fall to less than 200 g.

3. The crystallization is best accomplished by cooling for several hours at 0°. Cooling in an ice-salt mixture is much quicker but the erucic acid so obtained contains more oleic acid.

4. The centrifuge affords an easy way of filtering the erucic acid, since, if the acid is not quickly separated from the mother liquor, it melts and makes separation impossible. If a centrifuge is not available, the acid must be filtered at 0°, which is inconvenient except during cold weather.

5. The mother liquors from the recrystallizations may be combined, evaporated, and distilled under reduced pressure, taking two equal fractions. The lower (b.p. 200–220°/5 mm.) consists mainly of oleic acid; the higher (b.p. 220–230°/5 mm.) is solid at 20° and yields a further quantity of erucic acid on recrystallization.

6. The acid obtained contains a small percentage of arachidic acid and other higher saturated fatty acids, and has an iodine number of 66.9 (instead of about 75). If not entirely colorless, the product may be distilled under reduced pressure, when it boils at 241–243°/5 mm. or 252–254°/12 mm.; there is practically

no loss, only a minute amount of higher boiling material remaining in the flask.

3. Methods of Preparation

Erucic acid is a constituent of various natural oils but is most conveniently obtained from rape seed oil. The process described above is essentially that of Reimer and Will.[1] Methods have been developed for obtaining pure erucic acid free from saturated acids,[2] but these involve time-consuming procedures of fractional precipitation and crystallization, and necessarily give poor yields. The product obtained above is satisfactory for most purposes.

[1] Reimer and Will, Ber. **19**, 3320 (1886).

[2] Holde and Wilke, Z. angew. Chem. **35**, 105, 186, 289 (1922); Täufel and Bauschinger, *ibid.* **41**, 157 (1928).

XIX

ETHYL FUMARATE

$$\begin{array}{r} HCCO_2H \\ \| \\ HO_2CCH \end{array} + 2C_2H_5OH \rightarrow \begin{array}{r} HCCO_2C_2H_5 \\ \| \\ C_2H_5O_2CCH \end{array} + 2H_2O$$

Submitted by B. B. Corson, Elizabeth Adams, and R. W. Scott.
Checked by Henry Gilman and J. B. Dickey.

1. Procedure

The apparatus is assembled as shown in Fig. 2. Alcohol vapor from vaporizer flask *E* is passed through the acid contained in esterification flask *J*. The ester which is formed remains in *J* whereas the excess alcohol and the water formed during esterification continuously distil through column *K* into condenser *L* (Note 1). Flask *E* is a 250-cc. Pyrex distilling flask equipped with an extra side-arm *D*. Alcohol is run from dropping funnel *F* into flask *E*, a sufficient head being maintained by the height of funnel *G*. Stopcock *G′* is kept open, the flow of alcohol being regulated by stopcock *F′*. Side-arm *H* may be wrapped with asbestos paper to lessen condensation.

Side-arm *D* connects with two mercury safety valves, *C* and *B*. Tube *C′* dips about 3 cm. under the surface of the mercury contained in test tube *C*. This valve guards against excess internal pressure sometimes caused by the plugging of delivery tube *I*. Loud bubbling in the mercury quickly results from any clogging (Note 2) in the apparatus. Glass tube *A* (preferably a large capillary) barely dips into the mercury which just seals the bend of U-tube *B*. This valve guards against any fall of pressure within the system (Note 3), which would result in the transfer of the contents of flask *J* into vaporizer *E*, were it not compensated by the inrush of air through *A*. Since there is some lag

in this pressure compensation, the alcohol vapor delivery tube *I* should be about 30 cm. long; it should reach to within 2 or 3 cm. of the bottom of flask *J* and should extend about 10 cm. above the stopper of the flask. The delivery end may be drawn out to a coarse capillary (Note 4).

Esterification flask *J* is a 1-l. Pyrex round-bottom flask fitted with a 3-hole rubber stopper, carrying thermometer *T*, delivery

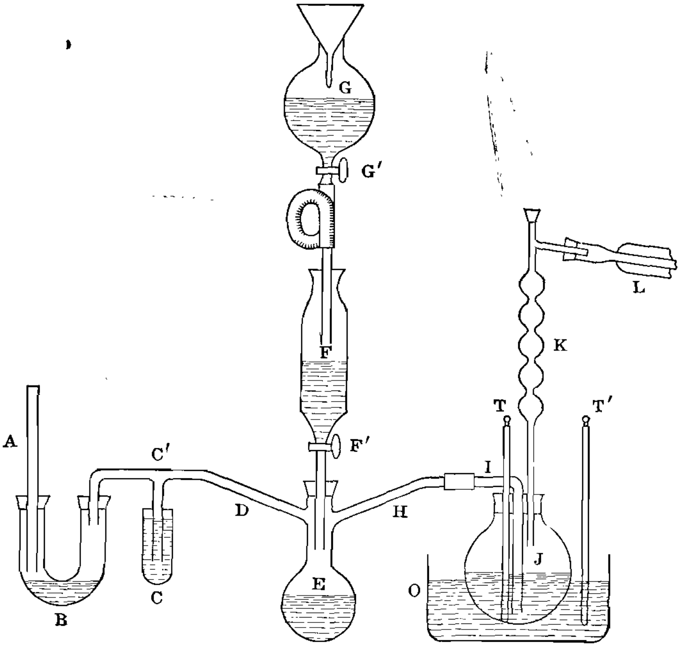


FIG. 2.

tube *I* and column *K*. Thermometer *T* should reach to within a few centimeters of the bottom of the flask, so as to register the temperature of the liquid esterification mixture. Flask *J* is immersed in and heated by the oil contained in deep dish *O*. Thermometer *T′* dips into the oil bath. Fractionating column *K* (Note 5) leads the vapor mixture of alcohol and water into condenser *L*.

Esterification flask *J* is charged with 348 g. (3 moles) of

fumaric acid and 350 cc. (Note 6) of 96 per cent ethyl alcohol containing 15 cc. of concentrated sulfuric acid. The oil bath is heated until the temperature of the reaction mixture in *J* is 110° (Note 7). During the preliminary heating about 200 cc. of alcohol distils from *J*. Then vaporizer *E* is heated over a gauze by a flame and the flow of 96 per cent (Note 8) alcohol (Note 9) from dropping funnel *F* is so regulated that the temperature of the esterification mixture in *J* remains between 115° and 120°, the temperature of the oil bath being maintained at about 150°. The reaction is stopped when 910 cc. of distillate has been collected; this requires about two hours.

The reaction mixture is then cooled to room temperature and neutralized with sodium carbonate solution (Note 10). The ester is separated and the aqueous layer shaken with benzene (Note 11); the liquids are combined, the benzene is distilled through a fractionating column (Note 12), and the ester from a side-arm flask at ordinary pressure, and the portion boiling at 213–215° is collected. The yield is 410 g. (80 per cent of the theoretical amount) (Note 13).

2. Notes

1. This preparation avoids the two disadvantages of the ordinary method of esterification by removing the water from the esterification mixture and by raising the reaction temperature.

2. If tube *I* clogs, the solid can often be blown out by temporarily raising test tube *C*, thereby increasing the pressure within the system.

3. Too rapid an addition of alcohol to *E* might cause a sudden fall of pressure.

4. The capillary tube *I* which delivers into flask *J* should be coarse, so as not to clog. With salicylic acid, which is especially prone to plug the delivery tube, the capillary end is omitted.

5. If a simple bent tube is used instead of a column, as much as 10 per cent of the ester may be carried over with the alcohol-water vapor.

6. The amount of alcohol to be added depends upon the

solubility of the acid in question. The esterification mixture when hot should be liquid enough to allow passage of the alcohol vapor. There should be no attempt to dissolve the acid completely. Complete solution occurs only after the esterification reaction has run for some time.

7. Should the acid tend to clog the delivery tube it is advisable to pass a slow stream of alcohol vapor through the esterification flask, in order to keep the tube open, even before the temperature of the esterification mixture has reached 110°.

8. If 99 per cent alcohol is used instead of 96 per cent, the yield of ethyl fumarate is 87 per cent of the theoretical instead of 80 per cent. When large quantities of ester are being prepared it is easy to use dry alcohol, since the alcohol-water distillate can be dehydrated over quicklime and used again. The wet alcohol is conveniently dehydrated by refluxing six hours over quicklime in a 12-l. flask and then distilling.

9. Methyl esters are easily prepared by substituting methyl for ethyl alcohol.

10. Sometimes a white solid precipitates when sodium carbonate solution is shaken with the esterification mixture. This solid usually dissolves if some water is added.

11. If the benzene solution of ester is to stand several hours before distillation it should be dried with a small amount of anhydrous sodium carbonate.

12. If the benzene is distilled from an ordinary distilling flask or through a simple bent tube some of the ester passes over with the benzene. The ester-benzene should be heated until the temperature at the top of the column is 110°.

13. This apparatus can be used in the preparation of various high boiling esters. Its development was assisted by a grant from the Cyrus M. Warren Fund of the American Academy of Arts and Sciences.

Following are the percentage yields obtained in the preparation of other esters; ethyl maleate, 73; ethyl salicylate, 70; ethyl oxalate, 80; ethyl benzoate, 92; methyl benzoate, 87. In the preparation of ethyl maleate troublesome emulsions were encountered in working up the product. Occasionally this hap-

pened with other esters. These emulsions can usually be broken by *suction filtration*. Salicylic acid esterifies more slowly than fumaric and requires a larger excess of alcohol.

3. Methods of Preparation

Various methods[1] of esterification, similar to the one described in the procedure, are to be found in the literature. In some methods[2] the process has been made continuous by passing the alcohol-water distillate through a dehydrator and then returning the vapor of the dried alcohol to the esterification mixture; in others,[3] a substance such as carbon tetrachloride, chloroform or benzene has been added, the water then being removed by means of a ternary mixture, for example, water-alcohol-benzene. When alcohol vapor is passed through the esterification mixture, as described above, the reaction temperature can be held as high as desired. The high temperature and the removal of water as fast as formed more than compensate for the absence of a large excess of alcohol.

Ethyl fumarate has been prepared from fumaric acid and ethyl alcohol, with or without sulfuric acid as catalyst,[4] from silver fumarate and ethyl iodide,[5] from silver maleate and ethyl iodide plus a trace of iodine,[6] from ethyl maleate by the action of iodine,[6] from ethyl maleate and phosphorus pentachloride,[7] and by passing hydrogen chloride into a boiling absolute alcohol solution of malic acid.[8]

[1] Lea, Am. J. Sci. (2) **39**, 210 (1865); Frankland and Duppa, Phil. Trans. Roy. Soc. London **156**, 310 (1866); Phelps and Hubbard, Am. J. Sci. (4) **23**, 368 (1907); Phelps and Phelps, Am. J. Sci. (4) **24**, 194 (1907); Kohler and Allen, Org. Syn. **3**, 54 (1923).

[2] Frankland and Aston, J. Chem. Soc. **79**, 517 (1901); Gibson, Proc. Roy. Soc. Edinburgh **28**, 703 (1908); Kenyon, Org. Syn. **5**, 59 (1925).

[3] Taylor, Proc. Roy. Soc. Edinburgh **25**, 831 (1905); Clarke and Davis, Org. Syn. **2**, 23 (1922); Wahl, Bull. soc. chim. (4) **37**, 715 (1925).

[4] Laubenheimer, Ann. **164**, 294 (1872); Purdie, J. Chem. Soc. **39**, 346 (1881); **47**, 856 (1885).

[5] Anschütz, Ber. **11**, 1645 (1878); **12**, 2282 (1879); Purdie, J. Chem. Soc. **39**, 346 (1881).

[6] Anschütz, Ber. **12**, 2282 (1879).

[7] Henry, Ann. **156**, 177 (1870).

[8] Laubenheimer, Ann. **164**, 295 (1872).

XV

ETHYL OXOMALONATE *

$$CH_2(CO_2C_2H_5)_2 + 2N_2O_3 \rightarrow CO(CO_2C_2H_5)_2 + 4NO + H_2O$$

Submitted by B. B. CORSON and R. K. HAZEN.
Checked by F. C. WHITMORE and F. L. CARNAHAN.

1. Procedure

THE apparatus is assembled according to Fig. 3. *A* is a 500-cc. Pyrex filter flask. *B* is a 2-l. three-neck round-bottom flask; into one of the side necks is fitted a 300-cc. dropping fun-

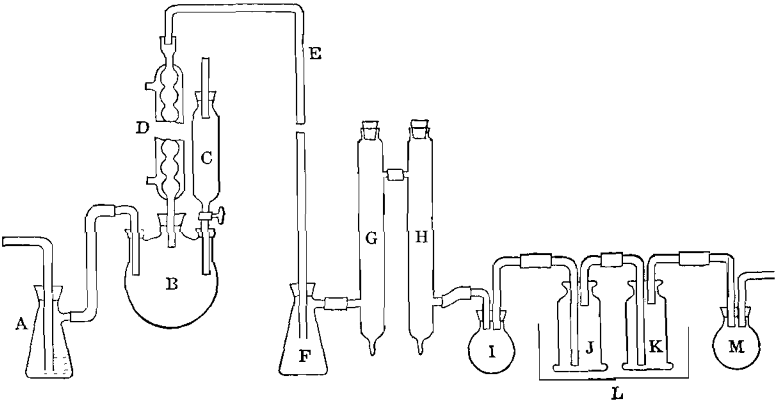


FIG. 3.

nel *C* (Note 1), and the second side neck is closed with a loose-fitting, well-greased rubber stopper, which serves as a safety valve against any sudden increase of pressure in the generator. A long (75-cm.) water-cooled bulb condenser *D* is connected to

* Apparatus for the reaction described in Org. Syn. **4**, 27.

the middle neck of the generator flask *B*. The large bore glass tube *E* connects the top of the condenser *D* with trap *F*, a 500-cc. filter flask, which is connected by means of a short rubber tube to the drying towers *G* and *H* (Note 2). These towers are conveniently made from glass condenser jackets; the bottom ends are sealed and the top ends closed with rubber stoppers (Note 3). Tower *H* is connected to " sight flask " *I*, a 500-cc. round-bottom flask. This in turn is connected to the absorption vessels *J* and *K* (500-cc. gas washing bottles), which are immersed in an ice-salt bath contained in dish *L*. Absorption bottle *K* is connected to " sight flask " *M*, a 500-cc. round-bottom flask similar to *I*. By means of the sight flasks *I* and *M* the efficiency of absorption can be judged by the depth of color. Flask *I* also serves to catch any liquid sucked back from the absorption vessels.

Before finally assembling the apparatus, the various units are charged as follows: *A* is one-third filled with water to serve as a bubble counter. Generator *B* is about one-quarter filled with dry arsenious oxide, pea size or powdered. Drying towers *G* and *H* are filled with anhydrous calcium chloride. (It is well to place a wad of glass wool in front of the entrance and exit tubes.) In each of the two absorption bottles *J* and *K* is placed 200 g. of ethyl malonate. Dish *L* is filled with an ice-salt freezing mixture.

When assembled as indicated, the apparatus is ready for operation. Concentrated nitric acid is run, in small portions, into generator *B* from dropping funnel *C*. After the action has started, the nitric acid must be forced into flask *B* by applying a small air pressure at the top of dropping funnel *C* and then opening the stopcock. Later on, when the gas generation slackens, flask *B* is heated with a smoky flame. The evolution of gas is maintained at a steady rate by increasing the heat until finally all the arsenious oxide has dissolved and the frothing has ceased. During the whole operation a slow stream of compressed air (Note 4) is passed through the apparatus from " bubble counter " *A*. The stream of air is insufficient if any colorless gas, which turns brown on coming in contact with the air, leaves the apparatus at *M*. When the arsenious oxide is exhausted, as shown

by a slackening in gas evolution, the old generator is removed and a fresh one put in its place. (If the generator is first allowed to cool somewhat, this change can be accomplished without much discomfort.) The moist oxides of nitrogen, in passing up through the condenser *D*, lose most of their moisture and the gas on passing down through tube *E* should deposit very little water in trap *F*. The gas is then thoroughly dried in the towers *G* and *H*. When the calcium chloride in *G* becomes wet (after several runs) the tower is refilled; at the same time *G* and *H* are interchanged. After passing through the drying towers and through flask *I*, the gas is absorbed by the cold ethyl malonate in vessels *J* and *K*. The ethyl malonate becomes dark green in color. There should be an increase in weight of about 200 g. in absorption bottle *J* in two or three hours (Note 5).

The rest of the directions are the same as in the original article by Dox (Note 6).

2. Notes

1. All the stoppers in this apparatus are of rubber, well greased with vaseline.

2. All rubber connections of this apparatus must be of thick tubing, well greased inside.

3. Ordinary gas-drying towers may also be used for *G* and *H*.

4. The reaction between arsenious oxide and concentrated nitric acid yields a mixture of nitric oxide and nitrogen dioxide. It also contains some nitrogen tetroxide and perhaps trioxide, the amount in equilibrium depending upon the temperature of the gas. The compressed air forced in via flask *A* insures an excess of oxygen, and thus complete oxidation. Only a slow stream is necessary, two to three bubbles per second.

5. A complete run should if possible be made without stopping. However, if the preparation must be stopped before completion, the absorption vessels should be disconnected, weighed, and protected against moisture by calcium chloride tubes. They lose weight on standing owing to decomposition of the intermediate compound.

6. Upon adding the calculated amount of water to ethyl oxomalonate, decolorization takes place immediately with evolution of heat, and on cooling a solid mass of ethyl dihydroxymalonate results. After recrystallization from chloroform the product melts at 56–57°. (Communicated by Elizabeth Gilman and T. B. Johnson.)

7. This work was assisted by a grant from the Cyrus M. Warren Fund of the American Academy of Arts and Sciences.

XVI

GLUTARIC ACID

$$CH_2O + 2CH_2(CO_2C_2H_5)_2 \xrightarrow{(C_2H_5)_2NH} CH_2[CH(CO_2C_2H_5)_2]_2 + H_2O$$

$$CH_2[CH(CO_2C_2H_5)_2]_2 + 4H_2O \rightarrow$$

$$CH_2(CH_2CO_2H)_2 + 4C_2H_5OH + 2CO_2$$

Submitted by T. J. OTTERBACHER.
Checked by F. C. WHITMORE and F. L. CARNAHAN.

1. Procedure

Ethyl Propane-α,α,γ,γ-tetracarboxylate.—To a mixture of 1600 g. (10 moles, 1510 cc.) of ethyl malonate (Note 1) and 400 g. of 40 per cent formalin (5.3 moles) in a 5-l. round-bottom flask, cooled to 5° by immersion in ice, is added 25 g. (35 cc.) of diethylamine. The mixture is then allowed to come to room temperature and remain for fifteen hours, after which the flask is heated under a reflux condenser on a boiling water bath for six hours. The aqueous layer is then separated, and the residue is distilled under reduced pressure (Note 2) from a 3-l. special Claisen flask (Org. Syn. I, 40). The ester distils at 190–200°/12 mm.(210–215°/20 mm.) The yield (Note 3) is 1000 g. (61 per cent of the theoretical amount).

Glutaric Acid.—A mixture of 125 g. (0.37 mole) of the above product, 125 cc. of concentrated hydrochloric acid and 125 cc. of water is heated (Note 4) in a 1-l. flask under a reflux condenser until it becomes homogeneous (six to eight hours). The contents of the flask are then evaporated to dryness, and the residual glutaric acid is transferred to a 100-cc. Claisen flask and distilled under diminished pressure. The fraction boiling at 185–195°/10 mm. is collected. It is moistened with water (Note 5) and heated gently, after which it is dried at 30°. On recrystallization from

benzene, it separates in colorless needles, m.p. 96–97°. The yield is 38–40 g. (76–80 per cent of the theoretical amount).

2. Notes

1. The ethyl malonate used was a fraction of the technical grade boiling over a 3° range under diminished pressure.

2. The ester is distilled slowly at first in order to vaporize the water at a temperature below 50°.

3. The high boiling residue (500 g.) is stated[1] to contain considerable amounts of ethyl pentanehexacarboxylate.

4. In order to prevent loss of material through the condenser by bumping, the flask should be heated in an oil bath at 115° or its contents stirred vigorously.

5. The product is moistened to convert any anhydride, formed at the high temperature of distillation, into the acid.

3. Methods of Preparation

The preparation of glutaric acid by the hydrolysis of trimethylene cyanide has been described in a previous article in this series,[2] which includes a bibliography of the literature. The present method is a modification of that of Knoevenagel.[3]

[1] Gault, Bull. soc. chim. (4) **11**, 380 (1912).
[2] Marvel and Tuley, Org. Syn. **5**, 69 (1925).
[3] Knoevenagel, Ber. **27**, 2346 (1894).

XVII

HEPTANOL-2

$$CH_3CO(CH_2)_4CH_3 \xrightarrow{Na + C_2H_5OH} CH_3CH(OH)(CH_2)_4CH_3$$

Submitted by F. C. Whitmore and T. Otterbacher.
Checked by Henry Gilman and H. J. Harwood.

1. Procedure

In a 3-l. round-bottom flask, fitted with an efficient Liebig condenser (100 × 1 cm.), 228 g. (2 moles) of methyl *n*-amyl ketone (Org. Syn. **7**, 60) is dissolved in a mixture of 600 cc. of 95 per cent alcohol and 200 cc. of water. One hundred and thirty grams (5.4 moles) of sodium in the form of wire is gradually added through the condenser. During the addition of the sodium the flask is cooled with running water (Note 1) so that the reaction does not become unduly violent (Note 2).

When the sodium has dissolved (Note 3), 2 l. of water is added and the mixture is cooled to 15°. The upper oily layer is then separated, washed successively with a mixture of 25 cc. of concentrated hydrochloric acid and 25 cc. of water and with water alone, dried over 20 g. of anhydrous sodium sulfate, and distilled with a fractionating column (Note 4). After a small forerun of low-boiling liquid, the pure heptanol distils at 155–157.5°. The yield is 145–150 g. (62–65 per cent of the theoretical amount).

2. Notes

1. If no cooling is used, condensation products are formed and the yield of heptanol is reduced considerably.

2. The temperature can be held conveniently below 30° by cooling with ice. Such cooling when accompanied by stirring is

particularly helpful during the early addition of the sodium (either as wire or in small pieces). With cooling and stirring, very little refluxing takes place and after the addition of about 60 g. of sodium the reaction slows down to such an extent that large amounts of sodium can be added at once without danger of excessive heating.

3. The time required for addition of the sodium may be significantly decreased by the use of mechanical stirring. Although the yield is not increased appreciably by stirring, frothing is prevented and for this reason the sodium may be added more rapidly. If the sodium fails to dissolve readily at the end of the reaction, more water may be added to the mixture.

4. The submitters used a Young column with 20 disks 3 cm. apart. The checkers used a Glinsky 3-bulb column.

3. Methods of Preparation

Heptanol-2 has been prepared by the action of *n*-amyl magnesium bromide on acetaldehyde,[1] and by the reduction of methyl *n*-amyl ketone in alcoholic solution by means of sodium.[2]

[1] Henry, Rec. trav. chim. **28**, 446 (1909).

[2] Thoms and Mannich, *Ber.* **36**, 2544 (1903); Pickard and Kenyon, J. Chem. Soc. **99**, 58 (1911).

XVIII

LAURYL ALCOHOL

$$C_{11}H_{23}CO_2C_2H_5 \xrightarrow{Na+C_2H_5OH} C_{11}H_{23}CH_2OH$$

Submitted by S. G. Ford and C. S. Marvel.
Checked by F. C. Whitmore and D. J. Loder.

1. Procedure

The central neck of a 5-l. three-neck round-bottom flask is fitted with a stopper carrying a mercury-seal mechanical stirrer. One of the side necks is connected by means of a short piece of heavy rubber tubing to a large reflux condenser about 2 m. long, with an inner tube 2.5 cm. in diameter (Note 1). The third neck is fitted with a separatory funnel.

In the flask are placed 70 g. (3 moles) of sodium and 200 cc. of dry toluene (Note 2). The flask is heated in an oil bath until the sodium is melted. The stirrer is then started and, when the sodium is finely divided, the oil bath is removed and the mixture allowed to cool. Stirring must be continued during the cooling in order to keep the sodium finely divided.

When the mixture has cooled to about 60°, there are added from the separatory funnel, first, a solution of 114 g. (0.5 mole) of ethyl laurate (Note 3) in 150 cc. of absolute alcohol (Note 4), then 500 cc. more of alcohol, as rapidly as is possible (Note 5) without loss of material through the condenser. The time required for the addition of the ester solution and the alcohol is less than five minutes, usually two or three minutes. When the reaction has subsided, the flask is heated on a steam bath until the sodium is completely dissolved (Note 6). The mixture is then steam distilled to remove the toluene and ethyl alcohol.

The contents of the flask are transferred to a separatory funnel while still hot and washed three times with 200-cc. portions of hot water to remove the sodium laurate (Note 7). The lauryl alcohol is extracted with ether from the cooled mixture and the washings. The combined ether extracts are washed with water, sodium carbonate solution, and again with water, and dried over anhydrous magnesium sulfate. The ether is evaporated and the lauryl alcohol distilled under diminished pressure. The yield is 60–70 g. (65–75 per cent of the theoretical amount) of a product boiling at 143–146°/18 mm. or 198–200°/135 mm. (Note 8).

2. Notes

1. The reaction is very vigorous, and unless the condenser has a wide bore finely divided sodium may be forced out the top and bad fires may result. The inner tube of the condenser may advantageously be made of brass or copper.

2. The toluene is dried by distillation; the first 10 per cent is discarded and the remainder is stored over sodium until used.

3. The ethyl laurate used was prepared by the alcoholysis of cocoanut oil and fractionation of the resulting esters. The material boiled at 127–132°/5 mm.

4. The grade of the absolute alcohol used in the reduction is very important. Alcohol dried over lime gives very poor yields. In these experiments the alcohol used was dried with magnesium methylate (Org. Syn. 7, 37).

5. The best yields are obtained when the reductions are carried out rapidly. If the reaction seems to be about to get out of control, the stirrer is stopped and the mixture is cooled with an ice pack.

6. If several reductions are being made, time will be saved by transferring the mixture at this point to another flask, thus having the original apparatus ready for another reduction.

7. Unless the sodium laurate is carefully removed, it causes troublesome emulsions.

8. Ethyl undecylenate has been reduced to undecylenyl alcohol (b.p. 123–125°/6 mm.) in 70 per cent yields; ethyl myristate

to myristyl alcohol (b.p. 170–173°/20 mm.; m.p. 39–39.5°) in 70–80 per cent yields; ethyl palmitate to cetyl alcohol (b.p. 178–182°/12 mm.; m.p. 48.5–49.5°) in 70–78 per cent yields by using this same procedure.

3. Methods of Preparation

Lauryl alcohol has been prepared by the reduction of the aldehyde with zinc dust and acetic acid;[1] by the reduction of esters of lauric acid with sodium and absolute alcohol[2] or with sodium, liquid ammonia, and absolute alcohol;[3] by the reduction of lauramide with sodium and amyl alcohol.[4] The method in the above procedure is essentially that described by Levene and Allen.[5]

[1] Krafft, Ber. **16**, 1718 (1883).

[2] Bouveault and Blanc, Bull. soc. chim. (3) **31**, 674 (1904); Ger. pat. 164,294 [Frdl. 8, 1260 (1905)]; Levene and Allen, J. Biol. Chem. **27**, 443 (1916); Marvel and Tanenbaum, J. Am. Chem. Soc. **44**, 2649 (1922); Adams and Marvel, Org. Chem. Reagents, Univ. of Ill. Bull., Vol. 20, No. 8, p. 54 (1922).

[3] Chablay, Compt. rend. **156**, 1021 (1913); Ann. chim. (9) **8**, 215 (1917).

[4] Scheuble and Loebl, Monatsh. **25**, 348 (1904).

[5] Levene and Allen, J. Biol. Chem. **27**, 443 (1916).

XIX

MALONONITRILE

$$CNCH_2CONH_2 + PCl_5 \rightarrow CH_2(CN)_2 + POCl_3 + 2HCl$$
$$2CNCH_2CONH_2 + POCl_3 \rightarrow 2CH_2(CN)_2 + HPO_3 + 3HCl$$

Submitted by B. B. Corson, R. W. Scott and C. E. Vose.
Checked by C. S. Marvel and J. Harmon.

1. Procedure

One hundred and fifty grams (1.8 moles) of pure cyanoacetamide (Org. Syn **9**, 36) is thoroughly mixed in a large (20-cm.) mortar with 150 g. (0.7 mole) of phosphorus pentachloride (Notes 1, 2 and 3). This mixture is transferred (Note 4) as quickly as possible to a 500-cc. Claisen flask equipped with a 360° thermometer and an air-intake tube (Note 5). The Claisen is connected by means of a double-length air condenser to a 250-cc. filter flask which in turn is connected to a water pump (Note 6) through a manometer.

After the system has been evacuated to about 30 mm. of mercury, the Claisen flask is immersed in a boiling water bath. The mixture melts and its color deepens to orange. Boiling commences (in about fifteen minutes) before the solid is completely melted and the pressure rises to about 150 mm., owing to the liberation of hydrogen chloride and phosphorus oxychloride (Note 7). When the evolution of gas has slackened, as indicated by the fall of pressure and the less vigorous boiling of the reaction mixture (thirty to thirty-five minutes), the receiver is changed. The distilling flask is removed from the boiling water bath, wiped dry, and immersed in an oil bath at 140° (Notes 8 and 9); the fresh receiver is placed in ice water

The malononitrile begins to distil at 113°/30 mm. (125°/50

mm.). The temperature of the oil bath is slowly raised over a period of twenty-five minutes to 180° (Note 10) and the nitrile collected between 113° and 125°. When the distillation has almost ceased, the oil bath is removed so as to prevent discoloration of the product (Note 11). The yield (Note 12) of crude nitrile is 80–95 g. (67–80 per cent of the theoretical amount). The nitrile may be purified by vacuum distillation (Note 13) with about 10 per cent loss; it is collected between 113° and 120°/30 mm. One distillation yields a water-clear liquid, which quickly freezes to an ice-like solid (Note 14) melting at 28–30°. The product has a faint odor resembling that of acetamide.

2. Notes

1. The phosphorus pentachloride should be of good quality —a dry solid.

2. The weights of the reactants correspond to the ratio of 5 molecules of amide to 2 molecules of pentachloride. The use of larger proportions of phosphorus pentachloride leads to lower yields.[3]

3. Phosphorus pentoxide has been used as dehydrating agent but the pentachloride method is much superior. With the pentoxide method there is always trouble due to the formation of a black, sticky mass which swells up during the latter part of the experiment and often disrupts the apparatus.

4. This transfer is greatly facilitated by the use of a 15-cm. (6-inch) glass funnel whose stem has been cut off and the hole enlarged to almost the size of the neck of the Claisen flask. The mixture is emptied into the body of the funnel and pushed through the large hole by means of a glass rod. Particular care should be exercised, for any considerable breathing of the fumes brings on a harsh cough which may last for several days. A gas mask should be worn.

5. To avoid plugging, the air-intake tube is not drawn out to a capillary.

6. An oil pump cannot be used because of the corrosive acid fumes.

7. Unless the phosphorus oxychloride is to be recovered, it is advisable to allow it to be carried away by the suction. This is easily accomplished if the receiver is not cooled.

8. If the initial temperature of the oil bath is below 140°, the nitrile distils too slowly (with consequent lowering of yield); if the temperature is above 140°, the nitrile comes over too fast. In the latter case, some nitrile condenses in the rubber tubes leading to the pump, thus clogging the line.

9. The flask should be immersed as far as possible in the oil (to within about 100 mm. of the top of the flask). This is important. A 1-gal. enamel-ware coffee-pot makes an excellent oil bath. An ordinary soldered vessel will not stand the temperature.

10. The temperature of the oil bath must not rise much above 180°, else the distillate becomes colored and violent bumping is apt to occur. The distillate should not be allowed to solidify in the condenser. This is most apt to occur during the first part of the distillation. The solid is easily melted by heating with a small flame.

11. The residue in the Claisen flask can be softened by water and broken up with a rod. The small amount remaining is easily removed with concentrated nitric or, preferably, concentrated sulfuric acid.

12. The keynote to success in this preparation is speed. Malononitrile is a sensitive substance and it must be removed from the reaction mixture as rapidly as possible. After experience with one or two runs the yields will consistently be better than 67 per cent.

13. Malononitrile can be distilled in small amounts (50 cc. or so) at ordinary pressure; the boiling point is around 220°. However, the longer heating necessary with larger amounts is apt to cause violent decomposition. In such a case the liquid darkens, boils spontaneously, and finally spurts from the flask in a cloud of white fumes and burning liquid; the latter partially solidifies to a brittle red solid.

14. Nitrogen determination indicates a purity of 99.5 per cent. The product remains colorless for at least one year if

stored in brown bottles protected from the light. If kept in ordinary bottles and exposed to the light, the nitrile quickly darkens.

15. This work was aided by a grant from the Cyrus M. Warren Fund of the American Academy of Arts and Sciences.

3. Methods of Preparation

Malononitrile has been prepared by the action of phosphorus pentoxide on malonamide[1] and on cyanoacetamide;[2] the above method is based upon that of Hesse.[3]

[1] Henry, Compt. rend. **102**, 1394 (1886).
[2] Henry, Compt. rend. **102**, 1395 (1886).
[3] Hesse, Am. Chem. J. **18**, 726 (1896).

XX

METHYL OXALATE

$$(CO_2H)_2 + 2CH_3OH \xrightarrow{H_2SO_4} (CO_2CH_3)_2$$

Submitted by EVERETT BOWDEN.
Checked by C. S. MARVEL and A. T. KOIDE.

1. Procedure

IN a 500-cc. Pyrex flask, fitted with a cork which loosely carries a glass mechanical stirrer and a separatory funnel, are placed 90 g. (1 mole) of anhydrous oxalic acid (Org. Syn. **1**, 67; **10**, 78) and 100 cc. of methanol (Note 1). Then while the mixture is rapidly stirred, 35 cc. of pure concentrated sulfuric acid (Note 2) is slowly added through the separatory funnel. The mixture is heated, if necessary (Note 3), nearly to boiling, then filtered as rapidly as possible through a 15-cm. filter paper placed in a slightly heated glass funnel, the filtrate being collected in a 500-cc. wide-mouth Erlenmeyer flask. The first flask is rinsed out with 40 cc. of hot methanol, which is poured through the filter paper. After twenty-four hours (Note 4) (at 15°) the crystals are filtered off with suction, sucked as dry as possible, pressed between filter paper and air-dried for a few minutes. The filtrate after cooling to about −10° is filtered rapidly, and the product dried as before. A total of 100–115 g. of material, slightly moist with sulfuric acid and melting at 50–52°, is obtained.

To recrystallize, the above product is dissolved in 100 cc. of redistilled methanol, filtered through a warm funnel and allowed to crystallize. After several hours the crystals are filtered off, and the filtrate treated as before. A total of 80–90 g. (68–76

per cent of the theoretical amount) of methyl oxalate, melting at 52.5–53.5° (Note 5), is obtained.

2. Notes

1. The methanol used is the commercial (almost acetone-free) grade known as Columbian Spirits. This material is redistilled for recrystallizing the methyl oxalate.

2. Less sulfuric acid than that employed gives a smaller yield, whereas larger quantities sometimes result in a product that gives difficulty in filtration. It is essential that the acid be added slowly and with vigorous stirring to prevent local superheating and darkening of the solution and product. Some commercial grades of methanol become quite dark in contact with sulfuric acid. The grade of methanol used here does not discolor, the filtrates being only light yellow.

3. Solution of the oxalic acid causes a sharp drop in temperature whereas solution of the sulfuric acid raises the temperature.

4. The major portion of the reaction is complete within a few minutes, but several hours are necessary for complete crystallization.

5. Larger batches give the same percentage yield as the one described. When several batches are to be run, the alcohol from the first recrystallization becomes the starting alcohol for the second batch, etc. This increases the yield somewhat.

3. Methods of Preparation

Methyl oxalate has been prepared by distilling a mixture of oxalic acid, methyl alcohol and sulfuric acid;[1] by dissolving anhydrous oxalic acid in hot methyl alcohol;[2] by esterifying oxalic acid with methyl alcohol, using anhydrous hydrogen

[1] Dumas and Peligot, Ann. chim. phys. (2) **58**, 44 (1835); Ann. **15**, 32 (1835); Nohler, Ann. **81**, 376 (1852).

[2] Erlenmeyer, Jahresb. **1874**, 572.

chloride as a catalyst;[3] by methanolysis of ethyl oxalate;[4] by passing vapors of dry methanol through hydrated oxalic acid until the water has been removed;[5] by a process in which the methyl alcohol-water mixture evolved from hydrated oxalic acid and methanol is dried over potassium carbonate and returned to the reaction flask.[6] The method described in the procedure is simpler than any of these and gives very satisfactory yields.

[3] Rising and Stieglitz, J. Am. Chem. Soc. **40**, 726 (1918).

[4] Pfannl, Monatsh. **31**, 316 (1914); Reimer and Dounes, J. Am. Chem. Soc. **43**, 950 (1921).

[5] Dutt, J. Chem. Soc. **123**, 2714 (1923).

[6] Kenyon, Org. Syn. **5**, 60 (1925).

XXI

m-NITROACETOPHENONE

$$C_6H_5COCH_3 + HNO_3 \longrightarrow m\text{-}NO_2C_6H_4COCH_3 + H_2O$$

Submitted by B. B. CORSON and R. K HAZEN.
Checked by ROGER ADAMS and W. W. MOYER.

1. Procedure

In a 1-l. wide-mouth Erlenmeyer flask, immersed in an ice-salt bath contained in a 2-gal. earthenware crock, is placed 150 cc. of concentrated sulfuric acid. The flask is equipped with an efficient mechanical stirrer, a small dropping funnel and a thermometer reaching almost to the bottom of the flask (Note 1). The stirrer is started, and when the sulfuric acid has cooled to ice temperature or below, 59 cc. (0.5 mole) of pure acetophenone is slowly dropped in from the dropping funnel at such a rate (about ten minutes for the addition) that the temperature does not rise above 5° (Note 2). After the reaction mixture has cooled, this time to about −7°, the cooled (15–20°) nitrating mixture, consisting of 40 cc. (0.65 mole) of nitric acid (sp. gr. 1.42 at 15.5°) (Note 3) and 60 cc. of concentrated sulfuric acid, is added through the dropping funnel at such a rate (100–120 drops per minute) that the temperature of the reaction mixture remains at 0° or lower (Note 4). After the nitrating acid has been added, stirring is continued for ten minutes longer and the contents of the flask are poured (Note 5) with vigorous manual stirring, into a mixture of 750 g. of cracked ice and 1500 cc. of water. The product separates as a yellow flocculent solid.

After the ice has melted, the product is filtered by suction and the somewhat sticky mass pressed as dry as possible. It is transferred to a mortar and triturated with three successive 300-cc. portions of cold water (to remove acid); it is then stirred to a mush with two successive 25-cc. portions of ice-cold ethyl

alcohol (to remove adhering oil); the solid is pressed dry on the suction filter after each of the five washings. The product is pressed on a porous plate, and when fairly dry (about one hour) is dissolved in 100–120 cc. of hot ethyl alcohol (Note 6). The dark solution is filtered quickly through a small suction funnel (Note 7) and the hot filtrate is poured slowly into 1000 cc. of cold water which is stirred vigorously (Note 8) with a stirring rod during the addition and for several minutes afterward. After standing a few minutes the yellow solid is filtered off by suction, washed with 200 cc. of cold water, sucked dry and pressed out on a porous clay plate.

When the reprecipitated *m*-nitroacetophenone (50–55 g.) is dry it is dissolved in 100 cc. of hot alcohol in a 300-cc. Erlenmeyer flask. The flask is then immersed in an ice bath and shaken vigorously while crystallization is taking place. Because of the great change in solubility between 60° and 50° the agitation of the liquid must be vigorous during this temperature interval, or large clumps of crystals will be formed instead of the purer and more easily dried mush. After the temperature has reached 20° (about one hour) the mixture is filtered by suction (Note 9). The solid (Note 10) is washed with 10 cc. of ice-cold alcohol and pressed dry on a clay plate. The product is light yellow; it softens at 74° and melts at 76–78°. The total yield is 45 g. (55 per cent of the theoretical amount).

2. Notes

1. The only flask found suitable for this preparation is the 1-l. wide-mouth Erlenmeyer. A large flask is necessary to insure rapid cooling. A propeller with long, wide blades agitates the viscous liquid much more efficiently than a stirrer of the centrifugal type. The blades should be as long as allowed by the wide mouth of the flask. The thermometer which is to record the temperature of the reaction mixture should enter at an angle and reach almost to the bottom of the flask, since the amount of liquid is small. The thermometer should have the zero point at least 15 cm. from the bulb in order to facilitate reading of the temperature. It is essential that the temperature

be watched throughout the experiment. A smaller ice-salt bath than that contained in a 2-gal. earthenware crock is inadequate.

2. The same dropping funnel can be used, without washing, for the addition of the concentrated sulfuric acid, the acetophenone and the nitrating mixture. With rapid stirring the acetophenone can be easily added in seven minutes without raising the temperature of the reaction mixture above 3°.

3. Nitric acid of lower specific gravity than 1.42 at 15.5° yields an impure product. Ordinary concentrated nitric acid usually has to be strengthened by the addition of fuming nitric acid.

4. *Two conditions are necessary for a good nitration: low temperature* (0° or below) and rapidity of addition of the nitrating mixture (not longer than forty-five minutes). With efficient cooling the temperature can be held between −5 and 0°. If the temperature should rise once or twice to 3° no harm is done provided the reaction mixture is quickly cooled back to the correct temperature. In order to avoid local heating the delivery tube of the dropping funnel should be so directed as to deliver the nitrating acid near the site of greatest agitation.

The rate of stirring must be rapid. The optimum speed will be different for different stirrers, depending on the shape and size of the blades. For the stirrer described the speed is 1600 r. p. m. During the addition of acetophenone this high speed is not necessary; in fact, it cannot be maintained on account of excessive splashing. However, during the addition of the nitrating acid the reaction mixture thickens and high-speed stirring becomes possible. The ice-salt mixture must be stirred repeatedly with a stick, and fresh ice and salt must be added from time to time. The temperature of the bath should be around −16°. Enough liquid should be present in the cooling bath so that the lower half of the flask is immersed in brine. If no especial care is exercised, the addition of the nitrating acid requires from two to three hours in order to maintain the temperature at 0° or below. This long exposure to the mixture of sulfuric and nitric acids is as harmful as a rise of temperature; the product is of poor quality and the yield drops from 55 to 15 per cent or less.

5. The experiment should not be stopped until the product has been poured into ice water.

6. Although 55° suffices to dissolve the *m*-nitroacetophenone it is desirable to bring the alcoholic solution to a boil to avoid crystallization during filtration.

7. Excessive frothing in the filter flask is easily checked by pinching off the suction tube from time to time.

8. Vigorous stirring and slow pouring are absolutely necessary. In the absence of either, the product will separate in a lumpy rather than in the flocculent form.

9. Since the solubility curve is so flat in the vicinity of room temperature it is not necessary to cool very low before filtering. The difference between 20° and 10° amounts to only 1 g. per 100 cc. of solution. The solubility of *m*-nitroacetophenone in 96 per cent alcohol is as follows:

Temperature	Weight in 10 cc.	Temperature	Weight in 10 cc.
8°	0.16	48°	1.88
17	0.25	50	2.38
22	0.31	52	3.08
23	0.34	53.5	4.05
27	0.41	56	5.46
28	0.45	57	8.05
32	0.64	59	11.00
39	0.97	60	15.60
42	1.22		

10. A small additional yield (about 5 g.) may be obtained from the mother liquor by concentrating to 20 cc. and then cooling in ice.

11. This work was aided by a grant from the Cyrus M. Warren Fund of the American Academy of Arts and Sciences.

3. Methods of Preparation

m-Nitroacetophenone has usually been prepared by the nitration of acetophenone;[1] it has also been made by the hydrolysis of *m*-nitrobenzoylacetoacetic ester.[2]

[1] Engler and Emmerling, Ber. **3**, 886 (1870); Buchka, Ber. **10**, 1714 (1877); Engler, Ber. **18**, 2238 (1885); v. Kostanecki and Tambor, Ber. **34**, 1691 (1901); Rupe, Braun and Lembrzuski, Ber. **34**, 3522 (1901).

[2] Gevekoht, Ann. **221**, 334 (1884).

XXII

OXALIC ACID (ANHYDROUS)

$$C_2H_2O_4 \cdot 2H_2O \rightarrow C_2H_2O_4 + 2H_2O$$

Submitted by Everett Bowden.
Checked by C. S. Marvel and E. H. Woodruff.

1. Procedure

A laboratory oven (Note 1) is equipped with as many clay plates or enameled pie plates or trays as it will accommodate and is adjusted to operate at 98–99° (Notes 2 and 3). When the temperature has become constant the plates are removed, rapidly covered with a layer (not over 3–4 mm. deep) of pulverized (Note 4) hydrated oxalic acid, and then quickly replaced in the oven. The temperature will drop slightly for a few minutes (Note 5). After the oven has regained the temperature for which it was adjusted, it is heated for two hours longer at this temperature. The product is then removed, crushed if slightly caked, and quickly bottled. The yield from 100 g. of hydrated oxalic acid is 69–70 g. (96–98 per cent of the theoretical amount) (Note 6). The product is 99.5–100 per cent pure, as indicated by titration with standard alkali.

2. Notes

1. Any type of oven may be used, but the automatic electric requires least attention. As many trays may be used as there are shelves in the oven. The trays are heated with the oven to decrease the subsequent first drop in temperature.

2. Some *slight* sublimation is always noticed, and the acid tends to cake. At higher temperatures heavy losses are caused by sublimation, and the caked material is very imperfectly dehydrated; there is also some darkening. Under the conditions given a white product is formed.

3. The dehydration is faster at higher temperatures. Numerous experiments showed that one hour and twenty minutes at a temperature of 113-115° gave a nearly theoretical yield of slightly colored material containing 97 per cent of oxalic acid. A one-hour heating at the same temperature gave a " yield " of 102 per cent containing 94 per cent of oxalic acid. This result applies to a C. P. starting material; technical acid gives somewhat less favorable results.

4. The acid should be powdered so that 50 per cent will pass a 60-mesh sieve and all will pass a 40-mesh sieve. A 9-inch plate can be used for about 50 to 100 g. of acid.

5. The oven temperature always drops a few degrees, owing to the cooling effect of the cold acid and the evaporation of a relatively large quantity of water. This drop in temperature is much less noticeable in a large oven than in a small one, and in one having thermostatic control in contrast to manual control.

6. The amount of material which may be dried will depend entirely on the size of the oven and the size and number of trays used. By repeating the runs several kilograms of material may be dried in a day with very little attention.

7. The success of this method of dehydration depends upon an exact control of all conditions specified.

3. Methods of Preparation

Oxalic acid is readily dehydrated by the use of carbon tetrachloride,[1] but this method has the disadvantage of complexity, relative slowness, and the use of relatively large quantities of carbon tetrachloride.

Most methods depend upon the direct removal of water from oxalic acid crystals by the application of heat.[2] The weakness of this lies chiefly in a lack of standardization.

[1] Hultman, Davis and Clarke, J. Am. Chem. Soc. **43**, 368 (1921); Clarke and Davis, Org. Syn. **1**, 67 (1921).

[2] Rising and Stieglitz, J. Am. Chem. Soc. **40**, 726 (1918); Orndorff, Lab. Manual of Org. Chem., 67 (1922); Kenyon, Org. Syn. **5**, 59 (1925).

XXIII

α-PHENYL-β-BENZOYLPROPIONITRILE

$$C_6H_5CH{=}CHCOC_6H_5 + HCN \rightarrow C_6H_5CH(CN)CH_2COC_6H_5$$

Submitted by C. F. H. ALLEN and R. K. KIMBALL.
Checked by J. B. CONANT and HELEN O'BRIEN.

1. Procedure

THE following preparation, through the filtration of the crude solid and washing with water, should be carried out in a hood with a good draft.

Into a 5-l. flask or bottle set in a water bath and fitted with a stirrer, thermometer, and separatory funnel, are placed 208 g. (1 mole) of benzalacetophenone (Note 1), 3.5 l. of 95 per cent ethyl alcohol (Note 2), and 60 g. (1 mole) (Note 3) of glacial acetic acid (Note 3). The mixture is warmed with stirring to 35°, and a solution of 130 g. (2 moles) of potassium cyanide in 375 cc. of water is added from the separatory funnel over a period of about fifteen minutes. The initial greenish color changes to yellow after the acetic acid has all reacted and the solution has become alkaline (Note 3). Stirring is continued for three hours, the temperature being maintained at 35°. During this time about half of the nitrile crystallizes. The flask is then loosely stoppered and left in a cool place for about fifty hours (conveniently out-of-doors in cold weather, but out of direct sunlight), after which the solid is filtered off and washed, first with 500 cc. of cold 50 per cent alcohol, and then with water until free from potassium cyanide (silver nitrate test). The yield of air-dried material melting at 125° is 220–227 g. (93–96 per cent of the theoretical amount). This product is sufficiently pure for most purposes, although it contains traces of a high-melting substance. If a product of higher melting point is

desired, it may be recrystallized from 1 l. of 95 per cent alcohol or 375 cc. of acetone. Pure phenylbenzoylpropionitrile melts at 127°.

2. Notes

1. Crude alkali-free, air-dried benzalacetophenone is used (Org. Syn. **2**, 1).

2. The preparation may be carried out in a more concentrated solution (1000 cc. of alcohol) with the same yield, but an inferior product is obtained. If this is done, it is best to stir for fifteen minutes at 50° after all the cyanide has been added and then cool in tap water. Since the product separates as an oil from a solution of this concentration, it is best to inoculate with a crystal of the nitrile.

3. If the solution becomes too alkaline, the nitrile formed will add to a second molecule of unsaturated ketone so readily that the product will consist almost entirely of a high-melting (284–286°) substance. For this reason it is essential to measure the acetic acid accurately; if too much is used, addition of hydrocyanic acid will not take place.

3. Methods of Preparation

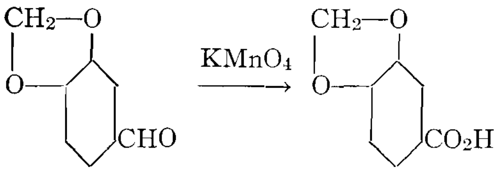
α-Phenyl-β-benzoylpropionitrile has been prepared by the action of sodium or potassium cyanide on β-chlorobenzylacetophenone,[1] and by the addition of hydrocyanic acid in the presence of sodium or potassium cyanide to benzalacetophenone.[2]

[1] Anschütz and Montfort, Ann. **284**, 2 (1895); Rupe and Schneider, Ber. **28**, 960 (1895).

[2] Hann and Lapworth, J. Chem. Soc. **85**, 1358 (1904); Lapworth and Wechsler, J. Chem. Soc. **97**, 41 (1910).

XXIV

PIPERONYLIC ACID



Submitted by R. L. SHRINER and E. C. KLEIDERER.
Checked by H. T. CLARKE and S. GRAFF.

1. Procedure

SIXTY grams (0.4 mole) of piperonal (Note 1) and 1500 cc. of water are placed in a 5-l. flask fitted with an efficient mechanical stirrer. The flask is placed on a steam bath and heated to 70–80° and the stirrer started. A solution of 90 g. of potassium permanganate in 1800 cc. of water is allowed to flow (Note 2) into the emulsion of piperonal and water (Note 3) over a period of forty to forty-five minutes. The stirring and heating are continued for an hour longer, at the end of which time the permanganate is reduced. A sufficient quantity of 10 per cent potassium hydroxide solution is added to make the solution alkaline. The mixture is filtered while hot and the manganese dioxide is washed with three 200-cc. portions of hot water. The combined filtrate and washings are cooled. At this point any unreacted piperonal that separates out must be filtered off (Note 4). The solution is now acidified with hydrochloric acid, the acid being added until no further precipitate forms. The resulting piperonylic acid is filtered off, washed with cold water until free of chlorides, and dried. The yield is 60–64 g. (90–96 per cent of the theoretical amount) of a colorless product melting at 224–225° (corr.). For most purposes the crude material is

pure enough, but it may be crystallized from ten times its weight of 95 per cent ethyl alcohol, yielding 52–56 g. (78–84 per cent of the theoretical amount) of needles melting at 227–228° (corr.).

2. Notes

1. The commercial grade of piperonal, m.p. 36°, may be used without purification.

2. The reverse order of addition lowers the yield to 50 per cent.

3. Vigorous mechanical stirring is necessary in order to emulsify the molten piperonal thoroughly with the water.

4. If the temperature of the reaction mixture is kept between 70° and 80° and the permanganate is added at the rate stated, the piperonal will be entirely oxidized.

3. Methods of Preparation

Piperonylic acid has been made by the oxidation of piperic acid,[1] piperonal,[1] safrole[2] and isosafrole[2] with potassium permanganate. It has also been prepared by the action of methylene iodide on protocatechuic acid [3] in the presence of alkali.

[1] Fittig and Mielck, Ann. **152**, 40 (1869).
[2] Ciamician and Silber, Ber. **23**, 1160 (1890).
[3] Fittig and Remsen, Ann. **168**, 94 (1873).

XXV

l-PROPYLENE GLYCOL

$$CH_3COCH_2OH + 2H \xrightarrow{\text{(Reductase of yeast)}} CH_3CHOHCH_2OH$$

Submitted by P. A. LEVENE and A. WALTI.
Checked by F. C. WHITMORE and J. PAULINE HOLLINGSHEAD.

1. Procedure

A SOLUTION of 1 kg. of sucrose in 9 l. of water is placed in a 20-l. bottle provided with a gas trap. A paste of baker's yeast (Note 1) is made by breaking up 1 kg. of yeast and gradually stirring in 1 l. of water. This is then added to the sugar solution and the mixture is allowed to stand at room temperature until a lively evolution of gas starts (from one to three hours). To the vigorously fermenting solution 100 g. of freshly prepared acetol (p. 1) is added, and the mixture is allowed to stand at room temperature until the reaction subsides (Note 2). The bottle is then transferred to an incubator at 32°, when the fermentation recommences. At the end of three days the reaction is generally completed, and the solution when tested with Fehling's reagent gives a negligible test for reducing sugars.

At this point 20–30 g. of short glass fiber or asbestos is added and the yeast is filtered out by suction. The filtrate is concentrated to a thick syrup under diminished pressure on a water bath, care being taken to keep the temperature below 40° (Note 3). The residue (about 200 cc.) is taken up in a mixture of 400 cc. of absolute alcohol and 100 cc. of dry ether (Note 4). The precipitate formed is removed by centrifuging, the supernatant liquid is decanted, and the residue is extracted with a mixture of 200 cc. of 98.5 per cent alcohol and 100 cc. of dry

ether (Note 5). The combined alcohol-ether solutions are concentrated under diminished pressure at 35–40° to a thick syrup. The residue is again taken up in a mixture of 400 cc. of 98.5 per cent alcohol and 100 cc. of dry ether and centrifuged (Note 5). The supernatant liquid is concentrated under diminished pressure and distilled from a modified Claisen flask (Org. Syn. 1, 40). The yield of the crude product boiling at 86–91°/12 mm. is approximately 100 g. The crude material is refractionated and collected at 88–90°/12 mm. or 187–189°/760 mm. The final product (Note 4) is a colorless liquid having a density 1.04 and specific rotation $[\alpha]_D^{20} = -15.0°$. The yield is 50–60 g. (49–58 per cent of the theoretical amount) (Note 6).

2. Notes

1. Fleischmann's yeast is satisfactory.

2. The addition of the acetol may cause the reaction to slacken for a time.

3. The evaporation must be carried out at as low a temperature as is practicable. A suitable device for vacuum evaporation of large volumes of liquid is given in Org. Syn. 4, 54.

4. The product reacts slightly acid. If an entirely neutral *l*-propylene glycol is desired, the syrup first obtained should be made neutral with a solution of sodium methylate in methyl alcohol, and again concentrated and extracted as indicated.

5. If a centrifuge is not available, about 15 g. of short glass fiber or asbestos may be added to the solution, stirred with a mechanical stirrer for five minutes or thoroughly shaken, and filtered on a suction filter with similar results to those obtained by centrifuging.

6. The optically active glycols are a convenient starting material for the preparation of optically active carbinols, hydroxy-acids, etc. The biological method of asymmetric reduction is perhaps the only convenient method for the preparation of these glycols. The steps in the preparation of other optically active glycols are identical with those of *l*-propylene glycol. In some cases it is found convenient to oxidize the chlorohydrin to the

corresponding chloroketone—the subsequent steps remaining the same as given above.

3. Methods of Preparation

l-Propylene glycol has been obtained from the optically inactive glycol by the action of bacteria,[1] and by means of strychnine compounds.[2] The present method is based on that of Färber, Nord and Neuberg.[3]

[1] LeBel, Jahresb. **1881**, 512.
[2] Grün, Ber. **52B**, 260 (1919).
[3] Färber, Nord, and Neuberg, Biochem. Z. **112**, 313 (1920).

XXVI

iso-PROPYL LACTATE

$$CH_3CHOHCO_2H + (CH_3)_2CHOH \rightarrow CH_3CHOHCO_2CH(CH_3)_2 + H_2O$$

Submitted by F. A. McDermott.
Checked by C. R. Noller.

1. Procedure

In a 3-l. round-bottom flask (Note 1) fitted with a 1-meter fractionating column [1] are placed 450 g. of anhydrous *iso*-propyl alcohol (Note 2), 212 g. (2 moles) of U. S. P. 85 per cent lactic acid, 1 l. of benzene, and 5 cc. of concentrated sulfuric acid. The flask is placed in an air bath on an electric hot plate (Note 3) and heated until the benzene-*iso*-propyl alcohol-water ternary mixture distils over at 66.5°. Distillation is continued slowly (six to seven hours) until the temperature at the head of the column rises to and persists at 71–72° (*iso*-propyl alcohol-benzene binary), and no further separation of water occurs. Ten grams of precipitated calcium carbonate is then added to the mixture, and distillation is continued until the temperature rises to 80° in order to remove most of the benzene and excess of *iso*-propyl alcohol (Notes 4 and 5). The contents of the flask are then filtered into a modified Claisen distilling flask (Org. Syn. **1**, 40) and the filtrate is distilled under reduced pressure. Cuts are taken to 60°, 60–75°, 75–80°, and 80–100° at 32 mm. The fraction boiling at 75–80°/32 mm. is *iso*-propyl lactate and weighs 130–160 g. By redistilling the high and low fractions an additional 30–60 g. is obtained, bringing the total yield to 160–180 g. (60–68 per cent of the theoretical amount). The ester may be redistilled at atmospheric pressure (with some loss due to decomposition) at 166–168°.

2. Notes

1. In large charges it is well to employ a two-neck flask, using the spare neck for introducing the calcium carbonate later in the process.

2. *Iso*-propyl alcohol is very difficult to dry satisfactorily. The water binary mixture, boiling at 80.35°, contains 12.1 per cent of water by weight. The ternary mixture with benzene, boiling at 66.5°, contains 73.8 per cent benzene, 18.7 per cent *iso*-propyl alcohol and 7.5 per cent water. Hence by adding 120 g. of dry benzene to 100 g. of the *iso*-propyl-water binary, and distilling off until the temperature reaches 82°, there will remain 55 to 60 g. of nearly dry *iso*-propyl alcohol. The commercial anhydrous alcohol was used in this preparation.

3. A water or steam bath or oil bath may be used.

4. The temperature of the vapors should not be allowed to rise above 72° before the addition of the calcium carbonate. If too much alcohol is removed before the acid is neutralized, charring and resinification take place with a decrease in the yield of ester.

5. The recovered benzene and excess *iso*-propyl alcohol may be dried by distillation and used in a subsequent run.

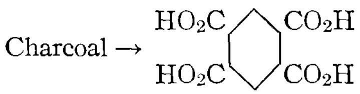
3. Methods of Preparation

Iso-propyl lactate has been prepared by heating *iso*-propyl alcohol and lactic acid in a sealed tube at 170°,[2] and from silver lactate and *iso*-propyl iodide, together with the *iso*-propyl ester of α-*iso*-propoxy-propionic acid.[3] Direct esterification of the acid with the alcohol, with sulfuric acid, has failed to give a yield greater than 20 per cent of the theoretical amount, and the product has been less pure.

[1] Clarke and Rahrs, Ind. Eng. Chem. **15**, 349 (1923).
[2] Silva, Bull. soc. chim. (2) **17**, 97 (1872).
[3] Purdie and Lander, J. Chem. Soc. **73**, 298 (1898).

XXVII

PYROMELLITIC ACID



Submitted by E. Philippi and R. Thelen.
Checked by H. T. Clarke and S. Graff.

1. Procedure

In a 5-l. round-bottom flask set on a wire gauze in a hood, and provided with a thermometer, are placed 100 g. of finely powdered pine or spruce charcoal (Note 1) and 650 cc. of 82–88 per cent sulfuric acid (sp. gr. 1.76–1.80) (Note 2) and a small drop of mercury (Note 3). The mixture is heated with a small flame and the temperature is raised to 250° during four hours. During another half hour the temperature is raised to 290°, when the acid begins to volatilize, and the mixture to froth and expand greatly (Note 4). During the next hour the temperature is raised to 300° and then to 315° during the following hour. Meanwhile the mixture has thickened somewhat. Then much bubbling and spurting take place and fine white needles of pyromellitic anhydride begin to collect in the neck of the flask (Note 5). Fifty cubic centimeters of sulfuric acid is now added, the walls of the flask being rinsed with it; after again being heated to 250° for a few minutes, the syrupy liquid is transferred to a 1000-cc. tubulated retort while still hot (Note 6). The flask is rinsed with the minimum amount of water and the washings are added to the retort. The water is first distilled off, then 30 g. of acid potassium sulfate is added to the mixture and the latter is heated vigorously with a free flame. At first almost colorless sulfuric acid distils. As soon as crystals of pyromellitic anhy-

dride appear, the receiver is replaced by one containing 50 cc. of water. The distillation is continued until nothing more passes over. At this point most of the pyromellitic anhydride has collected in the neck of the retort (Note 7). The retort is rinsed out with 100 cc. of water and the washings are filtered and evaporated on the steam bath to about 25 cc. The last distillate is also evaporated to 25 cc. On cooling, pyromellitic acid crystallizes. The product from both portions is collected on a suction funnel, using hardened filter paper, washed with two 10-cc. portions of ice water (Note 8) and recrystallized from four parts of boiling water. After drying at 105° the product (containing 2 moles of water of crystallization) melts at 271° (262° uncorr.). The yield is 6–8 g. (Note 9).

2. Notes

1. The yield of pyromellitic acid depends considerably on the kind of charcoal used. An experiment with ordinary willow charcoal gave none of the desired product.

2. The specific gravity of the acid used should not vary from the limits indicated.

3. A series of experiments has proved the helpful action of mercuric sulfate.

4. If the time for the first stage (temperature below 250°) is shortened, the frothing is greater at this point, and the final yield is lowered.

5. The end of the reaction can be readily detected by the bubbling and spurting which take the place of the quiet boiling. If the mixture is not fairly thick, less sulfuric acid should be used in the next run. If it is solid, more acid should be used.

6. The transfer to the retort must be made before the mixture solidifies. The best method of closing the tubulure of the retort (unless this consists of Pyrex glass) is by means of a glass stopper too small for the hole and wrapped with asbestos paper moistened with sodium silicate solution.

7. If considerable amounts of pyromellitic anhydride separate in the neck of the retort, it is advisable to rinse it into a

clean dish rather than into the receiver, which contains considerable sulfuric acid.

8. In recovering pyromellitic acid from the mother liquor it is advisable first to remove the sulfuric acid by adding a slight excess of barium hydroxide and acidifying to Congo red with hydrochloric acid.

9. The anhydride of pyromellitic acid may be obtained from the dry anhydrous acid by boiling with acetic anhydride.

3. Method of Preparation

Pyromellitic acid may be obtained by the oxidation of benzene derivatives containing organic substituents in the 1,2,4,5 positions: by the oxidation of durene with nitric acid;[1] by condensing benzene with diethyl malonyl chloride, reducing to the hydrocarbon, again condensing in the same way, and finally oxidizing the resulting tetraethyl benzodihydrindenedione;[2] and by an analogous synthesis from *m*-xylene, involving condensation with acetyl chloride, reduction and oxidation.[3]

Mellitic acid can be decarboxylated to yield pyromellitic acid, either by the action of heat alone[4] or in the presence of sulfuric acid.[5]

The oxidation of wood charcoal by means of sulfuric acid leads to mellitic acid and its decarboxylation products;[6] nitric acid may also be employed.[7] Pyromellitic acid has also been obtained by the electrolytic oxidation of graphite in an alkaline medium.[8]

[1] Jacobsen, Ber. **17**, 2516 (1884).

[2] Freund, Fleischer and Gofferjé, Ann. **414**, 26 (1918).

[3] Philippi, Seka and Froeschl, Ann. **428**, 300 (1922).

[4] Erdmann, Ann. **80**, 281 (1851); Baeyer, Ann. Suppl. **7**, 36 (1870).

[5] Erdmann, Ann. **80**, 282 (1851); Silberrad, J. Chem. Soc. **89**, 1795 (1906).

[6] Verneuil, Compt. rend. **118**, 195 (1894); **132**, 1340 (1901); Philippi and Thelen, Ann. **428**, 296 (1922).

[7] Silberrad, Ger. pat. 214,252, Frdl. **9**, 173 (1911); Philippi and Rie, Ann. **428**, 287 (1922).

[8] Bartoli and Papasogli, Gazz. chim. ital. **12**, 113 (1882); **13**, 37 (1883).

XXVIII

β-RESORCYLIC ACID

$$m\text{-}C_6H_4(OH)_2 \xrightarrow{CO_2 + KHCO_3} 1,2,4\text{-}C_6H_3(CO_2H)(OH)_2$$

Submitted by M. NIERENSTEIN and D. A. CLIBBENS.
Checked by ROGER ADAMS and F. E. KENDALL.

1. Procedure

IN a 5-l. flask fitted with a reflux condenser a solution containing 200 g. (1.8 moles) of resorcinol, 1000 g. (9.9 moles) of potassium acid carbonate (Note 1) and 2 l. of water (Note 2) is heated slowly on a steam bath for four hours. The flask is then placed over a flame and refluxed vigorously for thirty minutes; a rapid stream of carbon dioxide is passed through the solution during this heating process.

While still hot the solution is acidified by adding 900 cc. of concentrated hydrochloric acid (sp. gr. 1.19) from a separatory funnel with a tube delivering the acid to the bottom of the flask to prevent the formation of a layer of acid over the unneutralized solution. The flask is allowed to cool to room temperature and is then chilled in an ice-bath. The resorcylic acid crystallizes out in prisms, giving an almost colorless product which upon exposure to the air turns pink, owing to contamination with a small amount of resorcinol. The yield of crude acid is 225 g. By extracting the mother liquor with ether several times, 35 g. of resorcylic acid and some unchanged resorcinol can be recovered. The resorcylic acid is extracted from the ether by shaking with an aqueous solution of sodium bicarbonate. The aqueous solution is acidified with hydrochloric acid and again extracted with ether. The ether is then evaporated, leaving the resorcylic

acid, which is usually highly colored and must be recrystallized several times from boiling water and charcoal to remove the color.

The combined yield of crude acid (260–270 g.) is dissolved in 1 l. of water, boiled with about 25 g. of Norite, filtered through a heated filter, and crystallized by placing in an ice-salt freezing mixture and stirring vigorously. A finely crystalline, colorless product is obtained in this way. If it is allowed to crystallize slowly the crystals are somewhat colored. The yield of pure resorcylic acid melting at 216–217° is 160–170 g. (57–60 per cent of the theoretical amount) (Note 3).

2. Notes

1. Instead of potassium acid carbonate, the sodium salt in corresponding quantity may be used.

2. If less than ten parts of water to one of resorcinol is used, the yield is diminished.

3. The air-dried crystals lose at 110° a quantity of water corresponding to a half mole of water of crystallization.

3. Methods of Preparation

This method [1] of preparing β-resorcylic acid is a modification of the method given by Bistrzycki and Kostanecki.[2]

[1] Clibbens and Nierenstein, J. Chem. Soc. **107**, 1494 (1915).
[2] Bistrzycki and Kostanecki, Ber. **18**, 1984 (1885).

XXIX

SODIUM 2-BROMOETHANESULFONATE

$$BrCH_2CH_2Br + Na_2SO_3 \rightarrow BrCH_2CH_2SO_3Na + NaBr$$

Submitted by C. S. MARVEL and M. S. SPARBERG.
Checked by F. C. WHITMORE and D. J. LODER.

1. Procedure

IN a 5-l. round-bottom flask fitted with a reflux condenser, a mechanical stirrer, and a separatory funnel are placed 615 g. (3.27 moles) of ethylene dibromide (Note 1), 1250 cc. of 95 per cent alcohol and 450 cc. of water (Note 2). The stirrer is started and the mixture heated to boiling. To the well-stirred boiling mixture a solution of 125 g. (1 mole) of sodium sulfite (anhydrous salt) in 450 cc. of water is added through the separatory funnel over a period of about two hours. The solution is boiled under a reflux condenser for two hours after all of the sulfite solution has been added; the condenser is then set for distillation and the alcohol and the ethylene bromide are distilled (Note 3). The remaining water solution is poured into a large evaporating dish and evaporated to dryness on the water bath. The sodium 2-bromoethanesulfonate is extracted from the sodium bromide and unchanged sodium sulfite with 2 l. of boiling 95 per cent alcohol. On cooling the solution, most of the salt crystallizes and the mother liquor is used for a second extraction of the residue. The yield is 165–190 g. (78–90 per cent of the theoretical amount). The product (Note 4) may be further purified by recrystallizing from alcohol and drying in an oven at 110° (Note 5). The recovery on recrystallization is 75–80 per cent.

2. Notes

1. The large excess of ethylene dibromide is necessary to reduce the formation of the disulfonic acid.

2. The concentration of the alcohol seems to be important and poorer yields were obtained when it was changed in either direction.

3. By diluting the alcoholic distillate from the reaction mixture with 10 l. of water, it is possible to recover about 400 g. of ethylene dibromide.

4. This product may contain as much as 2 to 5 per cent of sodium bromide, but it is pure enough for the preparation of taurine (p. 98). A very pure product can be obtained by a second crystallization from alcohol.

5. The salt is slightly hygroscopic.

3. Methods of Preparation

The directions given in the procedure are based on those of Kohler.[1] No other practical method of preparation has appeared in the literature.

[1] Kohler, Am. Chem. J. **20**, 692 (1898); Marvel, Bailey and Sparberg, J. Am. Chem. Soc. **49**, 1836 (1927).

XXX

TAURINE

(2-Aminoethanesulfonic Acid)

$$BrCH_2CH_2SO_3Na + NH_3 \rightarrow NH_2CH_2CH_2SO_3H + NaBr$$

Submitted by C. S. MARVEL and C. F. BAILEY.
Checked by F. C. WHITMORE and D. J. LODER.

1. Procedure

A SOLUTION of 110 g. (0.52 mole) of sodium 2-bromoethanesulfonate (p. 96) in about 2 l. (28 moles) of concentrated aqueous ammonia (sp. gr. 0.9) is allowed to stand for five to seven days (Note 1) and is then evaporated to dryness. The last of the water is removed by heating on a steam bath. The residue is dissolved in the minimum quantity of hot water (about 500 cc.) and, if necessary, treated with 5 g. of decolorizing carbon (Norite). The colorless solution is concentrated to 65–70 cc., and 250 cc. of 95 per cent alcohol is added. In a short time taurine mixed with some sodium bromide separates. When crystallization is complete, the crude taurine is collected on a filter and recrystallized by dissolving in 100 cc. of hot water and then adding to the solution enough 95 per cent ethyl alcohol (about 500 cc.) to give a final concentration of 80 per cent of alcohol. The taurine which separates is usually free from bromides. However, occasional runs have to be recrystallized four or five times to remove all of the sodium bromide. The yield of pure taurine (Note 2) is 31–36 g. (48–55 per cent of the theoretical amount).

2. Notes

1. The reaction is about 25 per cent complete in five hours, 60 per cent complete in thirty hours, and 90 per cent complete in five days, as indicated by titration of the bromide ion.

2. The purity of the taurine prepared by this method was established by analysis.

3. Methods of Preparation

Taurine is generally prepared from ox bile[1] or the large muscle of the abalone.[2] It has been synthesized from isethionic acid through chloroethanesulfonic acid followed by the action of aqueous ammonia;[3] from ethyleneimine and sulfur dioxide;[4] from 2-mercaptothiazoline by oxidation with bromine water;[5] from bromoethylamine and ammonium sulfite;[6] and from acetaldehyde by a complex set of reactions involving sulfonation, formation of the aldehyde ammonia and the imido sulfonic acid and finally reduction.[7] The method given in the procedure has recently appeared in the literature.[8]

[1] Hammersten, Z. physiol. Chem. **32**, 456 (1901); Tauber, Beitr. Phys. Path. **4**, 324 (1904).

[2] Schmidt and Watson, J. Biol. Chem. **33**, 499 (1918).

[3] Kolbe, Ann. **122**, 42 (1862); Anschütz, Ann. **415**, 97 (1918).

[4] Gabriel, Ber. **21**, 2667 (1888).

[5] Gabriel, Ber. **22**, 1153 (1889).

[6] Reychler, Bull. soc. chim. Belg. **32**, 247 (1923).

[7] Auzies, Revue générale de chimie pure et appl. **14**, 278 [Chem. Zentr. **1911**, II, 1433].

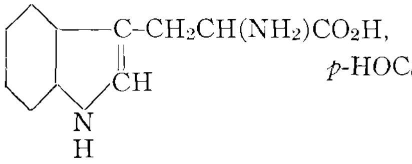
[8] Marvel, Bailey and Sparberg, J. Am. Chem. Soc. **49**, 1836 (1927).

XXXI

l-TRYPTOPHANE

(By-product, *l*-Tyrosine)

Digestion of Casein →



p-$HOC_6H_4CH_2CH(NH_2)CO_2H$

Submitted by GERALD J. COX and HARRIETTE KING.
Checked by H. T. CLARKE and JESSICA P. LELAND.

1. Procedure

Tryptophane.—In an 8-l. (2-gal.) bottle is placed 600 g. of commercial casein (coarse powder), which is then covered with about 3200 cc. of tap water at 37° (Note 1). The bottle is shaken until all of the casein is moistened. A solution of 60 g. of anhydrous sodium carbonate (Note 2) and 6 g. of sodium fluoride (Note 3) in 1 l. of water at 37° is added. A thin paste of 20 g. of commercial pancreatin in 100 cc. of water (37°) is poured in. The mixture is covered with a layer of toluene (80 cc.), diluted to 6 l., stoppered, shaken thoroughly, and placed in a warm room or bath at 37°.

After four or five days, with daily shakings, most of the casein is in solution and chalky masses of tyrosine begin to separate. After five days, a second dose of 20 g. of pancreatin in 100 cc. of water is added. After twelve days, the bottle is cooled in an ice-box over night and the undissolved material is filtered off (Note 4) and reserved for the preparation of tyrosine.

The filtrate (6900–7000 cc.) is measured into a 16-l. (4-gal.) stone jar and for every liter there is added 163 cc. of dilute sulfuric

acid (1 vol. of 95 per cent sulfuric acid and 1 vol. of water, cooled to room temperature). The first part of the acid must be added cautiously on account of the liberation of carbon dioxide.

The tryptophane is precipitated by adding a solution of 200 g. of mercuric sulfate (Note 5) in a mixture of 1860 cc. of water and 140 cc. of concentrated (95 per cent) sulfuric acid. After standing for twenty-four to forty-eight hours, the clear liquid is siphoned out and the yellow precipitate is filtered off and washed (Note 6) with a solution of 100 cc. of concentrated sulfuric acid in 1900 cc. of distilled water containing 20 g. mercuric sulfate, until the filtrate is colorless and Millon's test is atypical (Note 7); about 1500 cc. is necessary. The precipitate is washed with three successive 500-cc. portions of distilled water to remove most of the sulfuric acid.

The moist precipitate (120–130 g.) is suspended with mechanical stirring in 1200–1300 cc. of distilled water, and a hot, 20 per cent aqueous solution of barium hydroxide is added until the mixture is permanently alkaline to phenolphthalein (about 120 cc. is required). A rapid stream of hydrogen sulfide is passed in with stirring until the mercury is completely precipitated (Note 8). The precipitate is filtered off and washed with water until a sample of the washings gives a negative test for tryptophane with bromine water (Note 9). The barium is removed from the combined filtrate and washings by adding the exact amount of dilute sulfuric acid (Note 10) and filtering. The filtrate is concentrated under reduced pressure to about 80 cc.

The tryptophane is extracted from the aqueous solution by repeatedly shaking in a separatory funnel with 25-cc. quantities of *n*-butyl alcohol; water is added from time to time to keep the volume approximately constant (Note 11). The butyl alcohol extract is distilled under reduced pressure. After the water present has distilled over, the tryptophane precipitates in the distilling flask and may cause bumping. When all water has been removed, as is indicated by non-formation of drops on the side of the condenser, the distillation is stopped, and, after cooling, the tryptophane is filtered off and washed with a little fresh butyl alcohol. Such extractions and distillations are con-

tinued until the quantities of tryptophane obtained are negligibly small (Note 11).

The tryptophane so produced (7–8 g.) varies somewhat in quality in different runs. It is purified by recrystallization from 60 cc. of dilute alcohol (2 vol. of 95 per cent alcohol to 1 vol. of water), filtering off from the hot solution an appreciable quantity of insoluble matter and subjecting this to a second extraction with a further 10-cc. quantity of aqueous alcohol. The solution is decolorized by the addition of 1 g. of decolorizing carbon (Norite) and allowed to stand in the ice-box; the silvery leaflets of tryptophane are filtered off and washed successively with cold 70 per cent, 80 per cent, 95 per cent alcohol and finally with a little ether. Less than half the tryptophane is obtained in each crystallization (Note 12). The yield of pure (Note 13) tryptophane is 4.0–4.1 g., together with under 0.1 g. of less pure product.

Tyrosine.—The insoluble material (160–170 g.) obtained on filtering the digestion mixture is suspended in 320 cc. of water and 80 cc. of concentrated (36 per cent) hydrochloric acid, and the mixture boiled gently for thirty minutes (Note 14). After straining through cheese-cloth, decolorizing with 6 g. of Norite (Note 15) and filtering hot (Note 16), the warm (60–70°) solution is shaken with three 20-cc. portions of benzene (Note 17), and heated to boiling (Note 18). A slight excess (120–150 cc.) of 28 per cent ammonia is cautiously added, and the mixture is allowed to stand over night in the ice-box. The crystalline product is then filtered off and washed with three 40-cc. portions of ice-water. After drying, it weighs about 23 g. The mother liquor and washings are evaporated to about 200 cc., when a second crop is obtained, weighing slightly under 1 g.

The combined product is suspended in 400 cc. of water and dissolved by adding 8 g. of sodium hydroxide in 20–30 cc. of water (Note 19); 2 g. of Norite is added, and the solution filtered. The residue is washed on the funnel with 20–30 cc. of hot distilled water. The filtrate is heated to boiling (Note 18) and treated with 13 cc. of hydrochloric acid (Note 20), when crystallization usually begins. The mixture is then acidified to litmus with acetic acid (Note 21) and allowed to stand over night in the

refrigerator. The resulting tyrosine is filtered off and washed with ice-cold distilled water (130–150 cc. is necessary) until the washings are free of chloride. The product is dried in air or in a vacuum oven. The yield is 17.0–18.2 g. of pure white, silky needles of tyrosine. A second crop (about 0.5 g.) of a slightly less pure product may be obtained on concentrating the mother liquor to about 120 cc.

2. Notes

1. Tryptic action is more rapid if all water used is at 37°. Distilled water is not necessary at this stage.

2. This is a considerable excess of sodium carbonate. Smaller quantities might be satisfactory.

3. The sodium fluoride probably inhibits the action of the oxidases.

4. This filtration may be slow. Büchner funnels of 20-cm. diameter are best used; the preparation is allowed to suck dry from a single filling and the filter paper then changed.

5. Approximately this quantity of mercuric sulfate is necessary to precipitate the tryptophane completely, as judged by the Hopkins-Cole glyoxylic acid test.

6. This washing is to remove tyrosine, which is precipitated as a mercury compound somewhat more soluble than the tryptophane precipitate. The mercuric sulfate addition tends to reduce the tryptophane solubility.

7. A persistent red color is always obtained in the filtrates but the final color is distinctly different from that due to tyrosine.

8. Excess hydrogen sulfide must remain in the solution after standing. A sample of the filtrate, after acidifying with acetic acid, should give a copious black precipitate with lead acetate.

9. The bromine water test is somewhat more satisfactory for pure tryptophane than the glyoxylic acid test. Hydrogen sulfide may interfere (owing to sulfur formation) and must be boiled out first. The solution to be tested must be acid with acetic acid.

10. This amount is best determined in a 20-cc. aliquot sample, employing 2 per cent sulfuric acid in a burette.

11. In checking, it was found satisfactory to extract in a continuous apparatus (Fig. 4). Extraction is continued until the liquid in the flask begins to bump on account of the separation of solid; a new charge of butyl alcohol is then employed, about five charges being necessary. This process is repeated until the residue after a three-hour period of extraction fails to give the red color, characteristic of tryptophane, with bromine water. The time necessary will of course depend upon the rate of boiling; in checking, it was found to be twenty-eight to thirty hours.

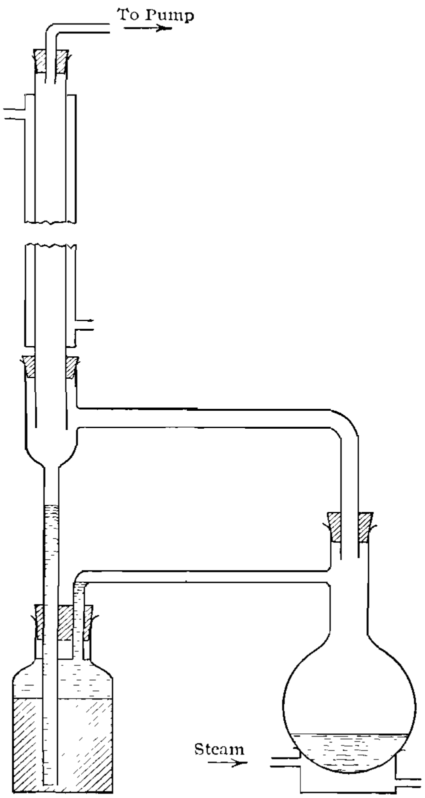


Fig. 4.

12. The recrystallization of the crude tryptophane is an extremely troublesome process. Not only must a less soluble by-product be removed, but the mother liquors contain a more soluble, gummy impurity in considerable proportion. After collecting each crop, the mother liquor must be evaporated to a small volume on the steam bath and treated with a double volume of alcohol. This process is repeated until no further crystals are obtained, but only a gum.

13. The purity of the tryptophane has been checked by the optical rotation ($[\alpha]_D = -28$ to $-33°$) and by analysis for amino nitrogen (6.8–6.9 per cent) by Van Slyke's method.

14. The boiling acid solution hydrolyzes protein material that otherwise greatly retards filtration.

15. The Norite used in this preparation is insufficient to decolorize the solutions completely, but gives a white final product.

16. All the filtrations in the purification of tyrosine, except possibly the last, are best done on a 20-cm. Büchner funnel. Whenever charcoal is used, kieselguhr may be employed to obtain a clear filtrate.

17. Benzene extracts traces of substances, probably fatty acid, that retard filtration and greatly alter the quality of the final product.

18. The tyrosine crystallizes in long, silky needles, easy to filter, if the solution is neutralized at the boiling point.

19. A small amount of flocculent impurity remains undissolved.

20. The hydrochloric acid is added to provide chloride ion as an index of complete washing.

21. Tyrosine is very slightly soluble in all concentrations of acetic acid. Therefore any excess of acetic acid does not redissolve the tyrosine.

3. Methods of Preparation

The above procedure for preparing tryptophane is an adaptation from the methods of Hopkins and Cole,[1] Dakin,[2] and Onslow.[3]

Tyrosine, as a primary product, may be readily prepared by hydrolyzing silk with hydrochloric acid, neutralizing the acid with sodium hydroxide, and finally acidifying with acetic acid.

[1] Hopkins and Cole, J. Physiol. **27**, 418 (1902).
[2] Dakin, Biochem. J. **12**, 302 (1918).
[3] Onslow, Biochem. J. **15**, 392 (1921).

APPENDIX

LATER REFERENCES TO PREPARATIONS IN PRECEDING VOLUMES

(The following references are to methods of possible preparative value that have been recently described. The numbers in parentheses following the name of a compound refer to the volume and page of Organic Syntheses.)

Acetal (3, 1):

(*a*) By the action of acetylene on alcohol in the presence of a mercury salt. Consortium f. elektrochem. Ind. Ges., Brit. pats. 257,622 and 264,791 (1925, 1926). [C. A. **21**, 3057 (1927); **22**, 243 (1928).]

(*b*) A study of the mechanism of the reaction. Adkins and Broderick, J. Am. Chem. Soc. **50**, 178 (1928).

Acrolein (6, 1):

By the action of heat on glycerol, using a " bleaching earth" catalyst such as "frankonite." Freund, U. S. pat. 1,672,378 (1928). [C. A. **22**, 2571 (1928).]

Adipic acid (5, 9):

By oxidizing cyclohexanol with nitric acid containing ammonium vanadate. Deutsche Hydrierwerke A. G., Ger. pat. 473,960 (1926). [C. A. **23**, 2988 (1929).]

dl-**Alanine** (9, 4):

By shaking a solution of ammonia and ammonium pyruvate with colloidal palladium in the presence of hydrogen, employing starch paste to stabilize the colloid. Aubel and Bourguel, Compt. rend. **186**, 1844 (1928).

Allyl alcohol (1, 15):

A study of the mechanism of the thermal decomposition of glyceryl formates; detailed directions for improved yields are

supplied. Delaby and Dubois, Compt. rend. **187**, 949 (1928); **188**, 710 (1929).

Arsonoacetic acid (**4**, 5):

By the action of chloroacetic acid on sodium arsenite; isolated and purified through the lead salt. Romberg and Ohman, Svensk. Kem. Tids. **36**, 119 (1924). [C. A. **19**, 36 (1925).]

Benzil (**1**, 25; **6**, 6):

By oxidizing benzoin in methyl alcoholic sodium methoxide solution by the addition of iodine. Corson and McAllister, J. Am. Chem. Soc. **51**, 2822 (1929).

Benzoic anhydride (**3**, 21):

(*a*) On treating benzoic acid with acetic anhydride at room temperature no mixed anhydride is formed, but benzoic anhydride separates with acetic anhydride of crystallization. van der Haar, Rec. trav. chim. **47**, 321 (1928).

(*b*) By treating benzotrichloride at 100–115° with water in the presence of certain heavy metal salts. Brit. Dyestuffs Corp., Ltd., Payman and Hall, Brit. pat. 280,373 (1926). [C. A. **22**, 2951 (1928).]

Benzoin (**1**, 33):

By the reduction of benzoic acid by means of magnesium and magnesium iodide. Gomberg and Bachmann, J. Am. Chem. Soc. **50**, 2762 (1928).

Benzophenone (**8**, 26):

(*a*) *o*-Benzoylbenzoic acid is heated with a small amount of its copper salt at 260°. Dougherty, J. Am. Chem. Soc. **50**, 571 (1928).

(*b*) By the action of carbon dioxide upon phenylmagnesium bromide. Ivanoff, Bull. soc. chim. (4) **43**, 441 (1928).

Benzyl benzoate (**2**, 5):

(*a*) Benzaldehyde is treated with aluminium ethoxide or butoxide, preferably in solution in an ester, such as an ethyl or butyl ester corresponding to the catalyst, or the molten catalyst

may be added to the benzaldehyde, the temperature allowed to rise, and the product distilled in vacuo. MATHESON, Brit. pat. 270,651 (1926). [C. A. **22**, 1597 (1928).]

(*b*) Benzaldehyde is treated with iodomagnesium butoxide in ether. The condensation runs to 45 per cent completion in five days. The product contains about 10 per cent of benzyl ether. GRIGNARD and FLUCHAIRE, Ann. chim. **9**, 19 (1928).

***n*-Butyl *n*-butyrate** (5, 23):

By the action of aluminium butoxide on butyraldehyde. SKIRROW, Can. pat. 279,974 (1928). [C. A. **22**, 2756 (1928).]

***n*-Butyl chloride** (5, 27):

By the action of hydrogen chloride on butyl alcohol under pressure at temperatures above 130° in silver or silver-lined vessels. BASEL and KAUFLER, Ger. pat. 462,993 (1928). [C. A. **22**, 4133 (1928).]

***n*-Butylmalonic ester (ethyl)** (4, 11):

The importance of using dry alcohol is emphasized. BHIDE and SUDBOROUGH, J. Indian Inst. Sci. A, **8**, 89 (1925). [Chem. Zentr. **1926**, I, 81.]

Catechol (3, 27):

(*a*) By treatment of a solution of phenol in sulfuric acid with sodium peroxide. MAGIDSON, POROZOVSKA and SELIGSOHN, Trans. Sci. Chem. Pharm. Inst. (Moscow) **6**, 23 (1923). [C. A. **22**, 3884 (1928).]

(*b*) By heating cellulose waste from wood, straw, etc. with alkaline solutions under pressure. MELANDER and WALLIN, Swed. pat. 62,831 (1927). [C. A. **21**, 4069 (1927).]

***o*-Chlorotoluene** (3, 33):

(*a*) By a modification of the Sandmeyer reaction. BRYD, Roczniki Chem. **7**, 436 (1927). [C. A. **22**, 2372 (1928).]

(*b*) Separation of the *o*- and *p*-isomers by selective sulfonation of the *o*- derivative at 90–120° for two to three hours. WAHL, U. S. pat. 1,596,325 (1926). [C. A. **20**, 3299 (1926).]

Cupferron (4, 19):

The addition of 0.05 g. of acetophenetidide to 100 cc. of cupferron reagent tends to prevent decomposition of the latter. GERMUTH, Chemist-Analyst **17**, no. 3, 3, 15 (1928). [C. A. **22**, 3372 (1928).]

Cyclopentanone (5, 37):

Similar to the method in Organic Syntheses, but barium oxide is used instead of barium hydroxide. VAVON and APCHIE, Bull. soc. chim. (4) **43**, 667 (1928).

***l*-Cystine** (5, 39):

By the hydrolysis of hair or completely defatted wool, followed by exact adjustment of the *p*H to 4.8. OKABE, J. Biochem. (Japan) **8**, 441 (1928).

Diacetone alcohol (1, 45):

By the action of potassium hydroxide or other suitable alkali upon acetone in benzene solution. The benzene represents a liquid miscible with the acetone, but not with the condensing agent. THOMSON, U. S. pat. 1,654,103 (1927). [C. A. **22**, 787 (1928).]

Diallyl cyanamide (5, 43):

The procedure described in Organic Syntheses. VLIET, U. S. pat. 1,659,793 (1928). [C. A. **22**, 1365 (1928).]

Di-*p*-tolylethane (4, 23):

By the reduction of α,α-di-*p*-tolylethylene with sodium in absolute alcohol. ANSCHÜTZ and HILBERT, Ber. **57**, 1699 (1924).

Ethyl *p*-aminobenzoate (8, 66):

By oxidation of acet-*p*-toluidide, followed by esterification of the *p*-aminobenzoic acid. CHEMNITIUS, Pharm. Zentralh. **68**, 765 (1927).

Ethyl oxomalonate (4, 27):

(*a*) Considerable amounts of oxomalonic acid (isolated as the sodium salt) are obtained by the action of nitric acid on

sucrose under carefully controlled conditions. CHATTAWAY and HARRIS, J. Chem. Soc. **121**, 2704 (1922).

(*b*) When dihydroxyacetone is heated in aqueous solution with cupric acetate, the product is chiefly oxomalonic acid. EVANS and WARING, J. Am. Chem. Soc. **48**, 2680 (1926).

Glutamic acid (5, 63):

(*a*) By the hydrolysis of gluten flour with hydrochloric acid and crystallization of the hydrochloride. The free acid is liberated from the hydrochloride by the action of aniline. ANSLOW and KING, Biochem. J. **21**, 1171 (1927).

(*b*) From beet sugar molasses residues. LARROWE CONSTRUCTION Co., Brit. pat. 265,831 (1926). [C. A. **22**, 509 (1928).]

Glycine (4, 31):

The preparation of glycine from chloroacetic acid by the action of ammonia has been improved so as to furnish a 63 per cent yield. ROBERTSON, J. Am. Chem. Soc. **49**, 2889 (1927).

Hydrazine sulfate (2, 37):

Hypochlorite solution is added, with stirring, to ammonia solution containing gelatin. MAGIDSON and FRENKEL, Trans. Sci. Pharm. Inst. (Moscow) **6**, 25 (1923). [C. A. **22**, 3881 (1928).]

Ketene (4, 39):

(*a*) Further details are given. HURD and TALLYN, J. Am. Chem. Soc. **47**, 1427 (1925).

(*b*) An apparatus for the preparation of small amounts of ketene from acetone is described. BILTZ, Z. angew. Chem. **36**, 232 (1923).

(*c*) Metallic sulfates are claimed to act as catalysts in the preparation of ketene in over 80 per cent yields from acetone. KETOID Co., Brit. pat. 237,573 (1924). [C. A. **20**, 1415 (1926).]

(*d*) By passing carbon monoxide and hydrogen over granular zinc oxide under pressure at 260–270°. DREYFUS, Brit. pat. 262,364 (1925). [C. A. **21**, 3626 (1927).]

(*e*) In 80 per cent yields by passing acetone vapor through a

copper tube packed with copper or silver turnings (to permit heat interchange) at 650–670°. No catalyst is necessary, but traces of nickel or iron bring about a secondary decomposition which greatly diminishes the yield. CLARKE and WARING, U. S. pat. 1,723,724 (1929). [C. A. **23**, 4485 (1929).]

Methylamine hydrochloride (3, 67):

By passing methyl alcohol and ammonia over thoria at 325–330°. DAVIS and ELDERFIELD, J. Am. Chem. Soc. **50**, 1786 (1928).

Methylene bromide (9, 56):

(*a*) In 80 per cent yields from bromoform and alkaline potassium arsenite. KOCHESKOV, J. Russ. Phys. Chem. Soc. **60**, 1191 (1928). [C. A. **23**, 2931 (1929).]

(*b*) A discussion of the mechanism of the reduction of bromoform by sodium arsenite. KOZESCHKOW, Ber. **61**, 1659 (1928).

α-Methyl *d*-glucoside (6, 64):

By boiling glucose for four and one-half hours with twice its weight of methyl alcohol containing 3 per cent of hydrochloric acid. PATTERSON and ROBERTSON, J. Chem. Soc. **1929**, 300.

Nicotinic acid (4, 49):

By oxidizing nicotine with potassium permanganate; purified by subliming in vacuo and crystallizing from water; m.p. when pure, 236–237° (corr.). SPÄTH and SPITZER, Ber. **59**, 1482 (1926).

***m*-Nitrochlorobenzene** (3, 79):

Nitrobenzene can be chlorinated at 40–50° by the use of 1 per cent of iron with 0.1 per cent of iodine as a combined catalyst. FIERZ-DAVID, Naturwiss. **17**, 13 (1929).

Nitrourea (5, 85):

A modification of the directions in Organic Syntheses which improves the yield. The amount of sulfuric acid is diminished and a method of recrystallization is given. DAVIS and BLANCHARD, J. Am. Chem. Soc. **51**, 1794 (1929).

Pentaerythritol (4, 53):

Essentially the process described in Organic Syntheses. Aaronson, U. S. pat. 1,678,623 (1928). [C. A. **22**, 3418 (1928).]

Pentene-2 (7, 76):

By reduction of the corresponding acetylene with hydrogen and colloidal palladium. Bourguel, Bull. soc. chim. **41**, 1475 (1927).

Phenylhydrazine (2, 71):

By reduction of benzenediazosulfonate with sulfur dioxide. Putokhin, Trans. Inst. Pure Chem. Reagents (Moscow) **1927**, 70. [C. A. **22**, 1337 (1928).]

β-**Phenylhydroxylamine** (4, 57):

(*a*) In 80 per cent yield by the action of ethereal hydrogen peroxide on $C_6H_5NHMgBr$ at $-25°$. Durand and Naves, Compt. rend. **180**, 521 (1925); Oddo and Binaghi, Atti accad. Lincei **32**, II, 349 (1923); Gazz. chim. ital. **54**, 193 (1924). [C. A. **18**, 3166 (1924).]

(*b*) By the reduction of nitrobenzene with sodium in liquid ammonia. White and Knight, J. Am. Chem. Soc. **45**, 1784 (1923).

n-**Propylbenzene** (4, 59):

(*a*) By the action of ethyl *p*-toluenesulfonate on benzylmagnesium chloride. Gilman and Beaber, J. Am. Chem. Soc. **47**, 523 (1925).

(*b*) Benzylmagnesium chloride is treated with β-chloroethyl *p*-toluenesulfonate, and the resulting γ-chloropropylbenzene is reduced by treating its Grignard reagent with water. Bert, Compt. rend. **186**, 373 (1928).

(*c*) By the action of ethylmagnesium bromide on benzyl chloride in boiling ligroin (70–90°) solution. Bert, Compt. rend. **186**, 587 (1928).

Pyrrole (9, 78):

Ammonium mucate is heated with an equal weight of glycerol; yields of 40–52 per cent of the theoretical amount are

obtained. The presence of an excess of ammonia is of no advantage. BLICKE and POWERS, Ind. Eng. Chem. **19**, 1334 (1927).

Pyruvic acid (4, 63):

The ethyl ester is prepared in 60 per cent yield by passing ethyl lactate with air or oxygen over a vanadium pentoxide catalyst. BOEHRINGER SOHN, U. S. pat. 1,614,195 (1927). [C. A. **21**, 746 (1927).]

Quinoline (2, 79):

The violence of the original Skraup procedure may be eliminated by the addition of 100 cc. of 80 per cent acetic acid for every 60 cc. of 95 per cent sulfuric acid. COHN and GUSTAVSON, J. Am. Chem. Soc. **50**, 2709 (1928).

***o*-Tolunitrile and *p*-tolunitrile** (4, 69):

(*a*) The process described in Organic Syntheses. CLARKE and READ, J. Am. Chem. Soc. **46**, 1001 (1924).

(*b*) Nickel cyanide is said to be better than copper cyanide in the preparation of nitriles by the Sandmeyer reaction. KORCZYNSKI and FANDRICH, Compt. rend. **183**, 421 (1926).

Tricarballylic acid (4, 77):

By heating propane-$\alpha,\beta,\beta,\gamma$-tetracarboxylic acid, and by hydrolysis of the ester of this acid. PERKIN and PINK, J. Chem. Soc. **127**, 191 (1925); GAULT and KLEES, Bull. soc. chim. (4) **39**, 892 (1926).

ADDITIONS AND CORRECTIONS FOR PRECEDING VOLUMES

(The numbers in parentheses following the name of a compound, refer to a number and page of Organic Syntheses.)

Adipic acid (9, 90): For 62,919 read 62,831.

Benzalacetone (3, 17). Following the directions, but replacing the benzaldehyde by an equivalent quantity (540 g.) of anisaldehyde, anisalacetone (b.p. 180–185°/18 mm., m.p. 72–74°) has been obtained in a yield of 83 per cent of the theoretical amount. The distillation residue, on recrystallization from ethyl acetate, yields 18 g. of dianisalacetone (m.p. 128–129°).

Ethyl cyanoacetate (9, 91). For Urushibana read Urushibara.

Nitromethane (9, 92). For Carcarras read Carcanas.

SUBJECT INDEX

(This Index Comprises Material from Volume X Only.)

(Names in capital letters refer to titles of individual preparations. Numbers in italics refer to preparative directions for substances formed either as principal products or as by-products; numbers in ordinary type indicate pages on which compounds or subjects are mentioned in connection with other preparations. For example: BROMOACETONE, 1, *12* indicates that bromoacetone is mentioned on page 1 and that directions for its preparation are given in detail on page *12*.)

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